STIC Search Report
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STIC Database Tracking Number: 182643

TO: Lalitha Nagubandi **Art Unit:** 1621 **Location:** rem/5D20/5C18 **Serial Number:** 10/750213 Friday, June 16, 2006	**From:** Beverly Shears **Location:** Biotech-Chem Library REM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

Search Notes

ACCESS DB # 142845

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[redacted] Approved

T. Page

SPE, AU 1621

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Lalitha Nagubandi Examiner #: 82043 Date: 06/14/06

Art Unit: 1621 Phone Number: 2-7996 Serial Number: 10/750,213 [redacted]

Location (Bldg/Room#): Rem 5D20 (Mailbox #): Rem 5C18 Results Format Preferred (circle): PAPER DISK

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MY

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Sulfonylalkanoylamino Hydroxyethylamino Sulfonamide useful as Retroviral Protease Inhibitors

Inventors (please provide full names): Michael L. Vazquez; Richard A. Mueller; John J. Talley; Daniel Getman, Gary A DeCresceno and John N. Freskos

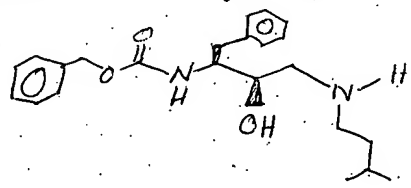
Earliest Priority Date: 1992/1993

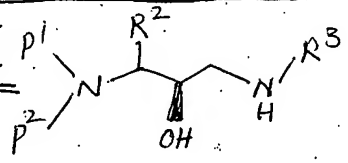
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Pleax search for str-/compd(s) N-[3(3)-benzyloxycarbonyl amino-2(R)-hydroxy-4-phenylbutyl]-N-isoamylamine.

I 

and also II 

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STAFF USE ONLY

Searcher: Beverly c 2528

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: _____

Searcher Prep & Review Time: _____

Online Time: _____

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation.

_____ Fulltext

_____ Other

Vendors and cost where applicable

✓ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial ____ Oligomer ____ Score/Length

____ Interference ____ SPDI ____ Encode/Transl

_____ Other (specify)

Nagybandi, L.
10/750213

FILE 'REGISTRY' ENTERED AT 16:24:46 ON 15 JUN 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JUN 2006 HIGHEST RN 887828-19-5
DICTIONARY FILE UPDATES: 14 JUN 2006 HIGHEST RN 887828-19-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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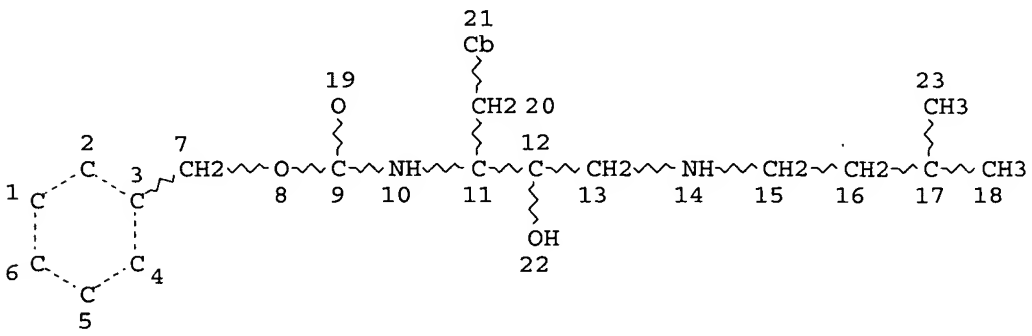
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1 STR



Str. I

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

Searcher : Shears 571-272-2528

STEREO ATTRIBUTES: NONE
L2 2 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 17556 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:24:46 ON 15 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 15 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 14 Jun 2006 (20060614/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

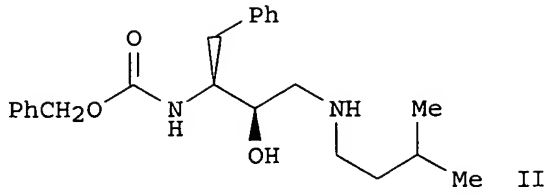
L3 42 L2

L3 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:23862 CAPLUS
DOCUMENT NUMBER: 136:85665
TITLE: Succinoylamino hydroxyethylamino sulfonyl urea derivatives useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Sun, Eric T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 32 pp., Cont. of U.S. Ser. No. 219,048, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

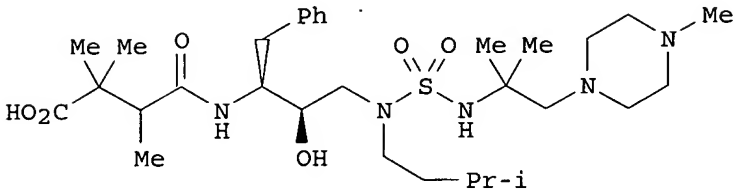
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6337398	B1	20020108	US 1995-542861	19951013
US 2002198378	A1	20021226	US 2001-11778	20011211
US 6515024	B2	20030204		
US 2004002542	A1	20040101	US 2002-315254	20021210
US 6951886	B2	20051004		
US 2006020009	A1	20060126	US 2005-183230	20050718
PRIORITY APPLN. INFO.:			US 1992-969682	B1 19921030

US 1994-219048	B1	19940328
US 1995-542861	A3	19951013
US 2001-11778	A1	20011211
US 2002-315254	A1	20021210

OTHER SOURCE(S): MARPAT 136:85665
GI



II



III

AB Intermediates used for the synthesis of title compds. R33R34X'-C:Y'-(CH2)pCR31R32-CR30R1-C:Y-NR6CHR2CHOHCH2NR3S(O)xNR4CR7R7'(CH2)nR8 [R1 = H, CH2SO2NH2, ester, amide, etc.; R2 = alkyl, aryl, cycloalkyl, etc.; R3 = (halo)alkyl, alken(yn)yl, hydroxyalkyl, etc.; R4 = H, R3; R6 = H, alkyl; R7-7' = H, R3, amino acid sidechains, etc.; R8 = CN, OH, alkyl, alkoxy, cycloalkyl, etc.; R30-32 = R1 or one of which combines with R1 to form a cycloalkyl radical; R33-34 = H, R1 or together with X' form a cycloalkyl radical; x = 1 - 2; X' = N, O, CR17, where R17 = H, alkyl; n = 0 - 6; p = 0 - 2; Y, Y' = O, S, NR15, where R15 = H, R3; I] were prepared For example, N-Cbz-L-phenylalanine chloromethyl ketone was reduced (MeOH/THF, -2°C, NaBH4), treated with base (EtOH, KOH) and the resulting epoxide intermediate reacted with isoamylamine (i-PrOH, reflux, 1.5 h) to give homochiral amine II in 31% yield for the 3 steps. II was elaborated by reaction with sulfamoyl chlorides/sulfamates, deprotected and functionalized with succinates to provide compds. I, e.g. claimed compound III. I are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease.

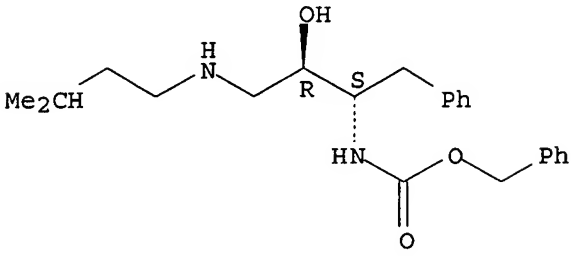
IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; succinoylamino hydroxyethylamino sulfonyl urea derivs. useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-

(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

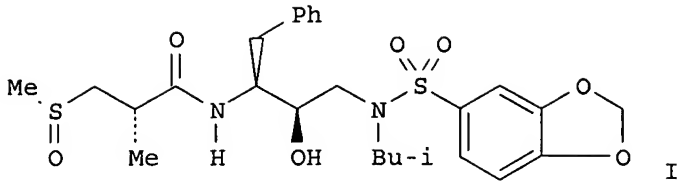
L3 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:10084 CAPLUS
DOCUMENT NUMBER: 134:71903
TITLE: Preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 401,838, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6169085	B1	20010102	US 1999-411374	19991004
US 6380188	B1	20020430	US 2000-672449	20000929
US 2003191166	A1	20031009	US 2002-82123	20020226
US 6667307	B2	20031223		
US 2004147758	A1	20040729	US 2003-677729	20031003
US 7045518	B2	20060516		

PRIORITY APPLN. INFO.:

US 1995-401838	B2	19950310
WO 1996-US2682	A1	19960307
US 1997-913069	A1	19971219
US 1999-411374	A1	19991004
US 2000-672449	A1	20000929
US 2002-82123	A1	20020226

OTHER SOURCE(S): MARPAT 134:71903
GI



I

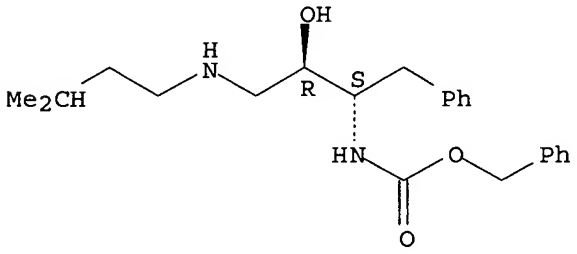
AB Sulfonylalkanoylamino hydroxyethylamino sulfonamide compds. R5S(O)t(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2SOMe, CH2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = benzo-fused heteroaryl or heterocyclyl; R5 = alkyl, alkenyl, alkynyl, aryl; t = 0-2) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-(methylsulfonyl)propanamide was prepared and assayed for HIV protease inhibitory activity (IC50 = 2 nM; EC50 = 20 nM). The corresponding methylsulfinyl derivative I (claimed compound) showed IC50 values 2 and 7 nM and EC50 values 52 and 80 nM for the two isomers.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:785899 CAPLUS
DOCUMENT NUMBER: 133:335236
TITLE: Preparation of hydroxyethylamino bis-sulfonamides as retroviral protease inhibitors
INVENTOR(S): Freskos, John N.; Getman, Daniel P.; Talley, John

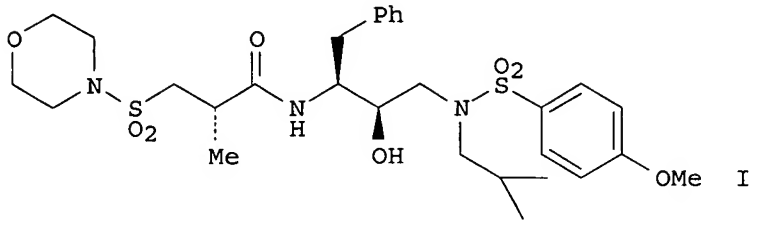
J.; Sikorski, James A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 60 pp., Cont.-in-part of U.S. Ser. No. 376,337, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6143747	A	20001107	US 1998-875025	19980226
WO 9622287	A1	19960725	WO 1996-US607	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
EP 1586558	A2	20051019	EP 2005-13695	19960118
EP 1586558	A3	20051026		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 6384036	B1	20020507	US 2000-635896	20000811
US 2003013751	A1	20030116	US 2002-76607	20020219
US 2004063771	A1	20040401	US 2003-417340	20030417

PRIORITY APPLN. INFO.:

US 1995-376337	B2	19950120
WO 1996-US607	W	19960118
EP 1996-902700	A3	19960118
US 1998-875025	A1	19980226
US 2000-635896	A1	20000811
US 2002-76607	A1	20020219

OTHER SOURCE(S): MARPAT 133:335236
GI



I

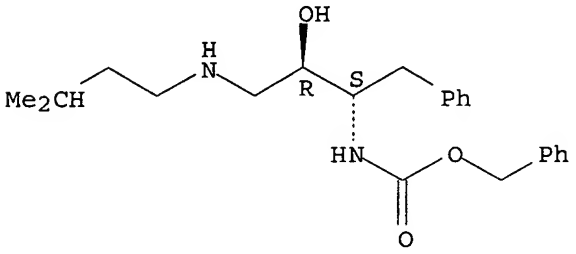
AB R10R11NSOw(CR7R8)tCHR1C(:Y)NR6CHR2CH(OH)NR3SOxR4 [R1 = H, CH2SO2NH2, CH2CO2Me, CO2Me, CONH2, alkyl, alkenyl, alkynyl, heterocyclyl, amino acid sidechain, etc.; R2 = (substituted) alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl, heteroaryl, heteroaralkyl; R3 = H, alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, heterocyclyl, heteroaryl, etc.; R4 = alkyl, haloalkyl, alkenyl,

alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, heteroaryl, heterocyclyl, etc.; R6, R8 = H, alkyl; R7 = CO2H, amidino, N-alkylamidino, R1; R1R7 = atoms to form a (heterocyclic) ring; R10, R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, arylcarbonylalkyl, thioalkyl, etc.; R10R11N = heterocyclyl, heteroaryl, etc.; x, w = 0, 1, 2; t = 0-6; Y = O, S, NH], were prepared Thus, 3-(N-morpholinosulfonyl)-2(R)-methylpropionic acid (preparation given) in DMF at 0° was treated with hydroxybenzotriazole and EDC followed by addition of 3S-amino-1-[N-(2-methylpropyl)-N-(4-methoxyphenylsulfonyl)amino]-4-phenyl-2R-butanol (preparation given) in DMF to give 67% title compound (I). This inhibited HIV-1 in CEM cells with IC50 = 10 nM.

IT **143225-04-1 159006-48-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydroxyethylamino bissulfonamides as retroviral protease inhibitors)

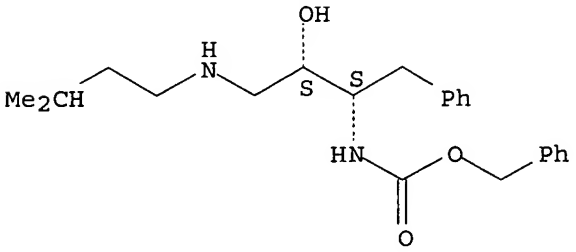
RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159006-48-1 CAPLUS
CN Carbamic acid, [(1S,2S)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:769109 CAPLUS
DOCUMENT NUMBER: 133:322130
TITLE: Synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid

hydroxyethylamine sulfonamide retroviral protease inhibitors

INVENTOR(S): Kunda, Sastry A.; Letendre, Leo J.; De Crescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 95 pp., Cont.-in-part of U.S. 5,756,533.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6140505	A	20001031	US 1998-80928	19980519
US 5756533	A	19980526	US 1995-474052	19950607
EP 1258491	A1	20021120	EP 2002-11526	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
WO 9959989	A1	19991125	WO 1999-US7047	19990518
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9938604	A1	19991206	AU 1999-38604	19990518
US 6310080	B1	20011030	US 1999-451920	19991201
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		
US 2003216435	A1	20031120	US 2002-200589	20020723
US 6730669	B2	20040504		
US 2004260095	A1	20041223	US 2004-760125	20040120

PRIORITY APPLN. INFO.:

US 1995-402287	B2	19950310
US 1995-474052	A2	19950607
US 1995-391873	B2	19950222
EP 1996-907135	A3	19960307
US 1998-80928	A1	19980519
WO 1999-US7047	W	19990518
US 1999-451920	A3	19991201
US 2001-836443	A1	20010418
US 2002-200589	A1	20020723

OTHER SOURCE(S): CASREACT 133:322130; MARPAT 133:322130

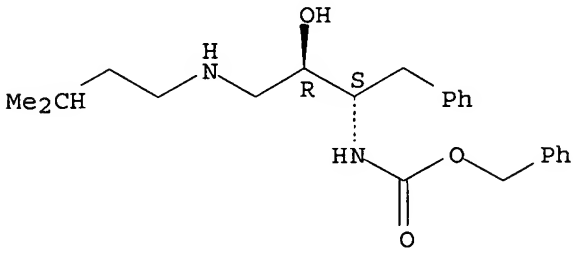
AB Benzo-fused heterocyclic sulfonyl halides for the preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors were obtained by a process comprising reacting a benzo-fused heterocyclic compound with an SO3 complex in the presence of a water immiscible, non-reactive solvent at 0-75°, cooling, if necessary, to a

temperature of from about -25° to about 65° and then adding oxalyl halide. Thus, N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-2S-[(pyrrolidin-1-yl)acetylamino]-3,3-dimethylbutanamide was prepared and shown to be an effective HIV protease inhibitor (IC50 = 3 nM, EC50 = 7 nM).

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

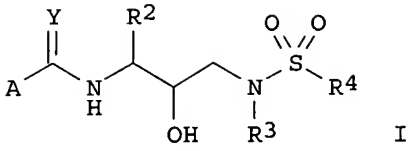
L3 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:304314 CAPLUS
DOCUMENT NUMBER: 132:322147
TITLE: Preparation of α- and β-amino acid hydroxyethylamino sulfonamides as retro viral protease inhibitors.
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Heintz, Robert M.; Bertenshaw, Deborah E.
PATENT ASSIGNEE(S): G.D.Searle and Co., USA
SOURCE: U.S., 93 pp., Cont.-in-part of Appl. PCT/US93/07814.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6060476	A	20000509	US 1994-204827	19940302
WO 9404492	A1	19940303	WO 1993-US7814	19930824

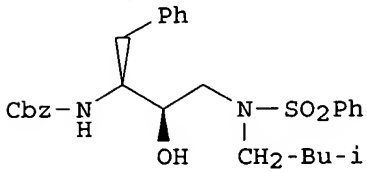
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,

	SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 810209		A2	19971203	EP 1997-113434	19930824
EP 810209		A3	19981202		
EP 810209		B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
WO 9506030		A1	19950302	WO 1994-US9139	19940823
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9476697		A1	19950321	AU 1994-76697	19940823
EP 715618		A1	19960612	EP 1994-927162	19940823
EP 715618		B1	19981216		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 174587		E	19990115	AT 1994-927162	19940823
ES 2127938		T3	19990501	ES 1994-927162	19940823
US 5968942		A	19991019	US 1994-294468	19940823
US 6455581		B1	20020924	US 1995-451090	19950525
US 6248775		B1	20010619	US 1999-288080	19990408
US 6500832		B1	20021231	US 2000-525161	20000314
US 2002052399		A1	20020502	US 2001-798255	20010305
US 6417387		B2	20020709		
US 2003191319		A1	20031009	US 2002-157019	20020530
US 6646010		B2	20031111		
US 2004044047		A1	20040304	US 2002-199481	20020722
US 6846954		B2	20050125		
US 6924286		B1	20050802	US 2003-633376	20030804
US 2004229922		A1	20041118	US 2004-812343	20040330
US 2005267171		A1	20051201	US 2005-110943	20050421
PRIORITY APPLN. INFO.:				US 1992-934984	B2 19920825
				WO 1993-US7814	A2 19930824
				EP 1993-923714	A3 19930824
				US 1993-110911	A 19930824
				US 1994-204827	A 19940302
				US 1994-294468	A1 19940823
				WO 1994-US9139	W 19940823
				US 1995-451090	A3 19950525
				US 1999-288080	A1 19990408
				US 2001-798255	A1 20010305
				US 2002-157019	A1 20020530
				US 2002-199481	A3 20020722
				US 2003-633376	A1 20030804

OTHER SOURCE(S): MARPAT 132:322147
GI



I



II

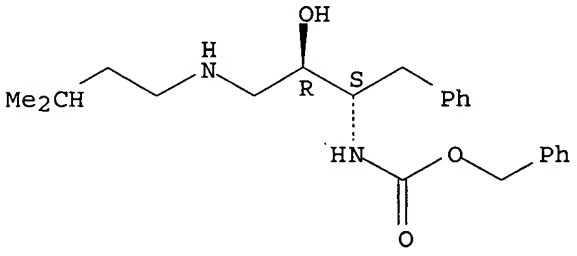
AB Amino acid hydroxyethylamino sulfonamide compds. I [R2 = (un)substituted aryl, (cyclo)alkyl, aralkyl, cycloalkylalkyl; R3 = alkyl, haloalkyl, alkenyl, alkynyl, hydroxy-, alkoxy-, alkylthio-, or alkylsulfonylalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, heterocycloalkylalkyl, aryl, aralkyl, or heteroaralkyl; R4 = heterocycloalkyl, heteroaryl or aryl; Y = O or S; A = heterocycloalkyl, heterocycloalkoxy, heterocycloalkylalkoxy, heteroaralkyl, heteroarylalkoxy, heteroaryloxy or heteroaryl] were prepared as retroviral protease inhibitors, particular as inhibitors of HIV protease. Thus, compound II (Cbz = benzyloxycarbonyl) was prepared and assayed for HIV inhibitory activity (IC50 = 16 nM). Compds. of formula I were tested for cytotoxicity and efficacy (IC50, EC50 and TD50 values at the nanomolar level are tabulated).

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:220728 CAPLUS

DOCUMENT NUMBER: 132:265504
TITLE: Preparation of hydroxyethylamino sulfonamides useful as retroviral protease inhibitors.
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Bertebshaw, Deborah E.; Heintz, Robert M.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 119 pp., Cont.-in-part of U.S. 204,872, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6046190	A	20000404	US 1996-586866	19960124
WO 9404492	A1	19940303	WO 1993-US7814	19930824
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 810209	A2	19971203	EP 1997-113434	19930824
EP 810209	A3	19981202		
EP 810209	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
WO 9506030	A1	19950302	WO 1994-US9139	19940823
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 1992-934984	B2	19920825
WO 1993-US7814	A2	19930824
US 1994-204872	B2	19940302
WO 1994-US9139	W	19940823
EP 1993-923714	A3	19930824
US 1993-110911	A	19930824
US 1994-204827	A	19940302

OTHER SOURCE(S): MARPAT 132:265504

AB Hydroxyethylamino sulfonamide compds. R9R10N(CR7R8)pCHR1C(:Y)NR6CHR2CH(OH)CH2NR3S(:O)xR4 [I: R1 = H, CH2SO2NH2, CH2CO2CH3, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, amino acid side chains, etc.; R2 = (un)substituted alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R3 = H, alkyl, haloalkyl, alkenyl, alkynyl, aryl, heteroaryl, mono- and disubstituted aminoalkyl, etc.; R4 = alkyl, haloalkyl, alkenyl, alkynyl, aryl, (un)saturated heterocycle, (un)substituted aromatic heterocycloalkyl, etc.; R6 = H, alkyl; Y = O, S, NR3; R7,R8 =

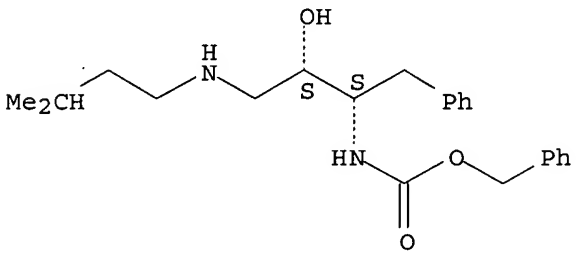
independently H, R1, or together with R1 and the carbon atoms to which they are attached represent a cycloalkyl radical; R9 = H, R3, or R3SO2; R10 = H, alkoxycarbonyl, alkylcarbonyl, aroyl, aryloxycarbonyl, heterocyclylalkoxycarbonyl, mono- and disubstituted aminocarbonyl, or aminoalkanoyl, etc.; or R9R10N = heterocycloalkyl or heteroaryl; x = 0-2; p = 0-1] or their pharmaceutically acceptable salts, prodrugs, or esters were prepared as inhibitors of retroviral proteases such as human immunodeficiency virus (HIV). Many inhibitors were prepared by (1) preparing an N-protected amino epoxide and (2) reacting this with an amine and (3) preparing a sulfonamide by reacting with a sulfonyl chloride or sulfonyl anhydride in the presence of an acid scavenger. The amino function of the sulfonamide was then (4) deprotected and (5) reacted with a carboxylate. Thus, N1-[2R-hydroxy-3-[(3-methylbutyl)(phenylsulfonyl)amino]-1S-(phenylmethyl)propyl]-2S-[(2-quinolinylcarbonyl)amino]butanediamide was prepared and assayed for HIV protease inhibitory activity (IC50 = 1.5 nM). Compds. of formula I were tested for cytotoxicity and antiviral efficacy (IC50, EC50, and TD50 values at the nanomolar level are tabulated).

IT **159006-48-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 159006-48-1 CAPLUS

CN Carbamic acid, [(1S,2S)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

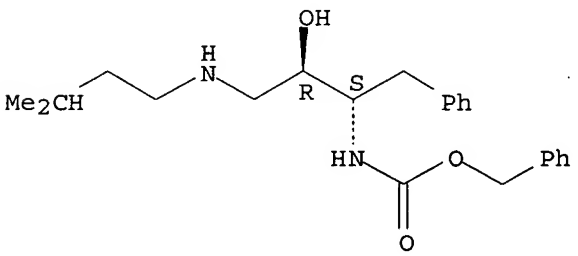


IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

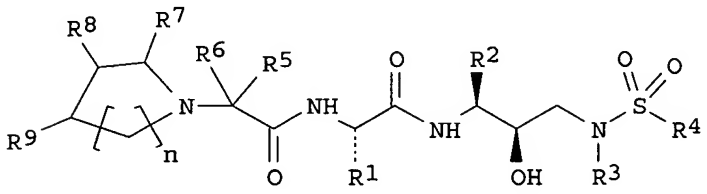
L3 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:753229 CAPLUS
DOCUMENT NUMBER: 132:6692
TITLE: benzo fused heterocyclo sulfonyl halide intermediates for the preparation of amino acids as HIV protease inhibitors
INVENTOR(S): Kunda, Sastry A.; Letendre, Leo J.; De Crescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959989	A1	19991125	WO 1999-US7047	19990518
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6140505	A	20001031	US 1998-80928	19980519
AU 9938604	A1	19991206	AU 1999-38604	19990518
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		

PRIORITY APPLN. INFO.:

US 1998-80928	A1	19980519
US 1995-402287	B2	19950310
US 1995-474052	A2	19950607
WO 1999-US7047	W	19990518
US 1999-451920	A3	19991201

OTHER SOURCE(S): MARPAT 132:6692
GI



I

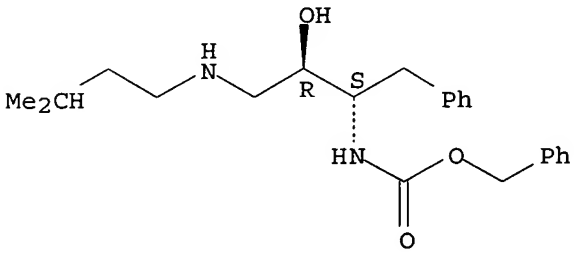
AB Sulfonyl amino acids I (R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, Ch2SOMe, Ch2SO2Me, CMe2SMe, CMeSOMe; R2 = alkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl; R3 = alkyl, cycloalkyl, cycloalkylalkyl; R4 = substituted heterocycle, R5 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R6 = H, alkyl, hydroxyalkyl, alkoxyalkyl, alkylamide, sulfone, alkylthioalkyl; R7-R9 = H, substituted heteroaryl, benzo) were prepared as HIV protease inhibitors. Process for preparing a benzo fused heterocyclo sulfonyl halide intermediate, comprising reacting a benzo fused heterocyclic compound with a -SO3- complex in the presence of a solvent and then adding oxalyl halide. Thus, amino acid I (R1 = CHMeEt, R2 = Bn, R3 = CH2CHMe3, R4 = Ph, R5-E9 = H, n = 1) was prepared and tested as HIV protease inhibitor (IC50 = 4 nM).

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(benzo fused heterocyclo sulfonyl halide intermediates for the preparation of amino acids as HIV protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:733035 CAPLUS

DOCUMENT NUMBER: 131:337352

TITLE: Preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors

INVENTOR(S): Getman, Daniel P.; DeCrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; McDonald, Joseph J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 401,838, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5985870	A	19991116	US 1997-913069	19971219
WO 9628418	A1	19960919	WO 1996-US2682	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 6380188	B1	20020430	US 2000-672449	20000929
US 2003191166	A1	20031009	US 2002-82123	20020226
US 6667307	B2	20031223		
US 2004147758	A1	20040729	US 2003-677729	20031003
US 7045518	B2	20060516		
PRIORITY APPLN. INFO.:			US 1995-401838	B2 19950310
			WO 1996-US2682	W 19960307
			US 1995-478625	A2 19950607
			US 1997-913069	A1 19971219
			US 1999-411374	A1 19991004
			US 2000-672449	A1 20000929
			US 2002-82123	A1 20020226

OTHER SOURCE(S): MARPAT 131:337352

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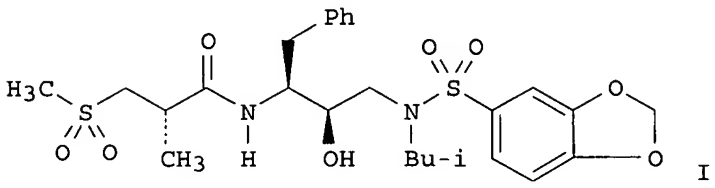


I

AB Sulfonylalkanoylamino hydroxyethylamino sulfonamide compds. R5S(O)t(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2SOMe, CH2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = benzo-fused heteroaryl or heterocyclyl; n, t = 0-2) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-(methylsulfonyl)propanamide (I) was prepared and assayed for HIV protease inhibitory activity (IC50 = 2 nM; EC50 = 20 nM).

IT **143225-04-1P**

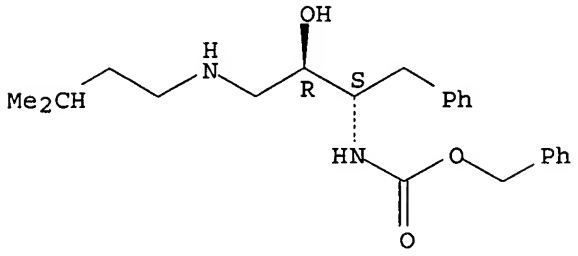
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

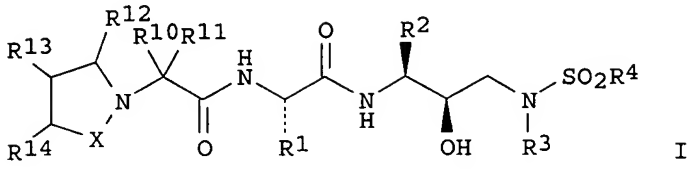
L3 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:671016 CAPLUS
DOCUMENT NUMBER: 131:286828
TITLE: Preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan R.; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 96 pp., Cont.-in-part of U.S. Ser. No. 402,287, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968970	A	19991019	US 1998-894900	19980102
WO 9628463	A1	19960919	WO 1996-US2684	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
EP 1258491	A1	20021120	EP 2002-11526	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		

PRIORITY APPLN. INFO.: US 1995-402287 B2 19950310
WO 1996-US2684 W 19960307
US 1995-474052 A2 19950607
EP 1996-907135 A3 19960307

US 1999-451920 A3 19991201

OTHER SOURCE(S): MARPAT 131:286828
GI



I

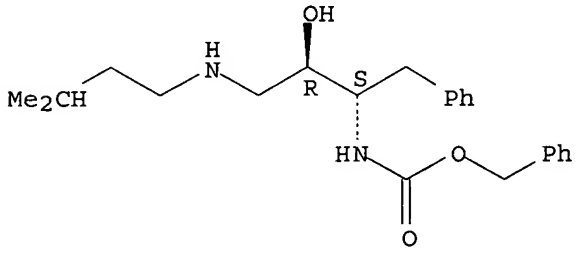
AB Amino acid hydroxyethylamino sulfonamide compds. I [X = CH2, CH2CH2; R1 = alkyl, alkenyl, alkynyl, hydroxy-, alkoxy-, or cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2S(O)Me, CH2SO2Me, CMe2SMe, CMe2S(O)Me, CMe2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl; R10 = H, alkyl, hydroxy- or alkoxyalkyl; R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl, benzyl, imidazolylmethyl, CH2CH2CONH2, CH2CONH2, CH2CH2SMe, CH2SMe, CH2S(O)Me, CH2SO2Me; R12 = H, hydroxyalkyl, alkoxyalkyl; R13, R14 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, or alkoxyalkyl or R13 and R14 together form (un)substituted benzo or heteroaryl] or their pharmaceutically acceptable salts, prodrugs, or esters were prepared as retroviral protease inhibitors. Thus, 2S-(pyrrolidinoacetamido)-N-[2R-hydroxy-3-[N1-(2-methylpropyl)-N1-(2,3-dihydrobenzofuran-5-ylsulfonyl)amino]-1S-(phenylmethyl)propyl]-3S-methylpentanamide was prepared and showed IC50 = 2 nM for inhibition of HIV protease.

IT **143225-04-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:670116 CAPLUS

DOCUMENT NUMBER: 131:295568
TITLE: α- and β-Amino acid hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazques, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Bertenshaw, Deborah E.; Heintz, Robert M.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 130 pp., .Cont.-in-part of U. S. 204,827.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968942	A	19991019	US 1994-294468	19940823
WO 9404492	A1	19940303	WO 1993-US7814	19930824
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 810209	A2	19971203	EP 1997-113434	19930824
EP 810209	A3	19981202		
EP 810209	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 6060476	A	20000509	US 1994-204827	19940302
US 6248775	B1	20010619	US 1999-288080	19990408
US 2002052399	A1	20020502	US 2001-798255	20010305
US 6417387	B2	20020709		
US 2003191319	A1	20031009	US 2002-157019	20020530
US 6646010	B2	20031111		
US 6924286	B1	20050802	US 2003-633376	20030804
US 2005267171	A1	20051201	US 2005-110943	20050421

PRIORITY APPLN. INFO.:		
US 1992-934984	B2	19920825
WO 1993-US7814	A2	19930824
US 1994-204827	A2	19940302
EP 1993-923714	A3	19930824
US 1993-110911	A2	19930824
US 1994-294468	A1	19940823
US 1999-288080	A1	19990408
US 2001-798255	A1	20010305
US 2002-157019	A1	20020530
US 2003-633376	A1	20030804

OTHER SOURCE(S): MARPAT 131:295568
AB α- And β-Amino acid hydroxyethylamino sulfonamide compds. are effective as retroviral protease inhibitors, and in particular as

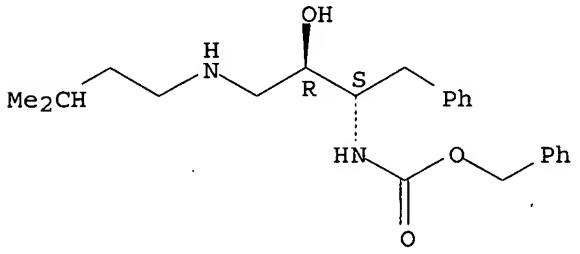
inhibitors of HIV protease, as well as effective in preventing the growth of retroviruses in a solution General and specific schemes for chemical synthesis of the sulfonamide-containing hydroxyethylamine inhibitor compds. are described. Seventy-eight such compds. were tested for cytotoxicity and antiviral efficacy (IC50, EC50, and TD50 values at the nanomolar level are tabulated).

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(α- and β-amino acid hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:799692 CAPLUS
DOCUMENT NUMBER: 130:38712
TITLE: Preparation of α- and β-amino acid hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 67 pp., Cont.-in-part of U.S. Ser. No. 934,984, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5843946	A	19981201	US 1993-110911	19930824
EP 810209	A2	19971203	EP 1997-113434	19930824
EP 810209	A3	19981202		
EP 810209	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 172717	E	19981115	AT 1993-923714	19930824
ES 2123065	T3	19990101	ES 1993-923714	19930824
AT 218541	E	20020615	AT 1997-113434	19930824

PT 810209	T	20020930	PT 1997-113434		19930824
ES 2177868	T3	20021216	ES 1997-113434		19930824
WO 9506030	A1	19950302	WO 1994-US9139		19940823
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN					
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9476697	A1	19950321	AU 1994-76697		19940823
EP 715618	A1	19960612	EP 1994-927162		19940823
EP 715618	B1	19981216			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
AT 174587	E	19990115	AT 1994-927162		19940823
ES 2127938	T3	19990501	ES 1994-927162		19940823
FI 9500650	A	19950214	FI 1995-650		19950214
FI 112471	B1	20031215			
US 5786483	A	19980728	US 1995-487662		19950607
US 5830897	A	19981103	US 1995-473698		19950607
US 6172082	B1	20010109	US 1995-476788		19950607
US 5744481	A	19980428	US 1997-845392		19970425
US 6248775	B1	20010619	US 1999-288080		19990408
US 6335460	B1	20020101	US 2000-510189		20000222
US 6472407	B1	20021029	US 2000-511005		20000222
US 6534493	B1	20030318	US 2000-694785		20001024
US 2002052399	A1	20020502	US 2001-798255		20010305
US 6417387	B2	20020709			
US 2003191319	A1	20031009	US 2002-157019		20020530
US 6646010	B2	20031111			
US 6924286	B1	20050802	US 2003-633376		20030804
PRIORITY APPLN. INFO.:			US 1992-934984	B2	19920825
			EP 1993-923714	A3	19930824
			US 1993-110911	A	19930824
			WO 1993-US7814	A2	19930824
			US 1994-204827	A	19940302
			US 1994-294468	A1	19940823
			WO 1994-US9139	W	19940823
			US 1995-476788	A1	19950607
			US 1995-485524	B1	19950607
			US 1999-288080	A1	19990408
			US 2001-798255	A1	20010305
			US 2002-157019	A1	20020530

OTHER SOURCE(S): MARPAT 130:38712

AB Amino acid hydroxyethylamino sulfonamide compds.
P1NHCHR2CH(OH)CH2NR3SO2R4 [P1 = alkoxycarbonyl, aralkoxycarbonyl, alkanoyl, cycloalkylcarbonyl, cycloalkylalkoxycarbonyl, cycloalkylalkanoyl, aralkanoyl, aroyl, aryloxycarbonyl,

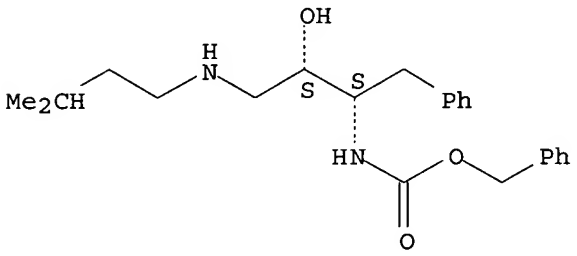
heterocyclylcarbonyl, heterocyclyloxycarbonyl, heterocyclylalkoxycarbonyl, heteroaralkoxycarbonyl, heteroaryloxycarbonyl, heteroaroyl; R2 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, (un)substituted aralkyl; R3 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heteroaryl, heterocyclylalkyl,. aryl, aralkyl, heteroaralkyl; R4 = alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, heteroaryl, aryl, aralkyl] were preparation as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[[(4-methoxyphenyl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-4-pyridinecarboxamide was prepared by amidation of isonicotinoyl chloride hydrochloride with 2R-hydroxy-3-[(2-methylpropyl)[(4-methoxyphenyl)sulfonyl]amino]-1S-(phenylmethyl)propylamine. Protease inhibitory data are tabulated.

IT **159006-48-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 159006-48-1 CAPLUS

CN Carbamic acid, [(1S,2S)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

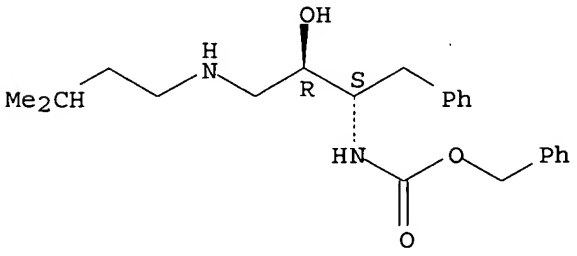


IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searcher : Shears 571-272-2528

L3 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:719136 CAPLUS
DOCUMENT NUMBER: 129:343424
TITLE: Macrocyclic hydroxyethylamine-type retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Chrusciel, Robert A.
PATENT ASSIGNEE(S): Monsanto Company, USA
SOURCE: U.S., 17 pp., Cont. of U.S. Ser. No. 48,720, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5830888	A	19981103	US 1995-406614	19950320
PRIORITY APPLN. INFO.:			US 1993-48720	B1 19930416

OTHER SOURCE(S): MARPAT 129:343424
GI

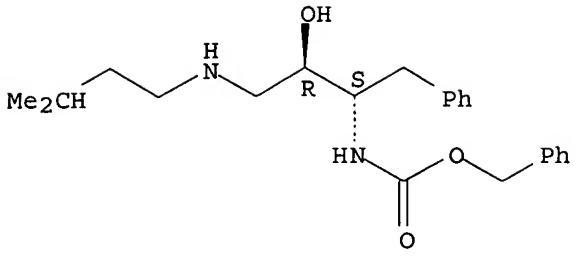
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to N-heterocycle-containing macrocyclic hydroxyethylamine protease inhibitor compds., compns. containing them, and methods for inhibiting retroviral proteases using them. In particular, compds. I are claimed [wherein R = H, alkoxycarbonyl, alkyl, aryl, and various acyl groups, etc.; m, p = 0, 1; R2 = (un)substituted alkyl, aryl, cycloalkyl, cycloalkylalkyl, and aralkyl; R2', R2'' = H, R2, CO2R, CH2CO2R, CH2CONH2, CH2SO2Me; R3 = alk(en/yn)yl, hydroxyalkyl, heteroaryl, aryl, (un)substituted aminoalkyl, etc.; n = 1-5; R4, R5 = H, R2; X = O, S, CH2, NR1; R1 = H, alkyl; X' = CH2, S, SO, SO2, R10NH; R10 = (CH2)qCO; q = 0, 1; R6 = H, alkyl]. Twelve examples were prepared and tested as HIV protease inhibitors. For instance, 6-bromohexanoic acid was converted to an isocyanate and reacted with an amine intermediate to give the intermediate II. This underwent a sequence of hydrogenolytic deprotection, coupling with N,S-bis-Z-cysteine by the mixed anhydride method, and S-deprotection in liquid NH3, with concomitant cyclization, to give title compound III. The latter had an IC50 of 570 nM against HIV protease in vitro.

IT **143225-04-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of macrocyclic hydroxyethylamine retroviral protease inhibitors)

RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:471469 CAPLUS
DOCUMENT NUMBER: 129:122867
TITLE: Heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; DeCrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 75 pp., Cont.-in-part of U. S. Ser. No. 402,419, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776971	A	19980707	US 1995-474117	19950607
CA 2215022	AA	19960919	CA 1996-2215022	19960307
WO 9628465	A1	19960919	WO 1996-US2683	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9654178	A1	19961002	AU 1996-54178	19960307
AU 717598	B2	20000330		
EP 815124	A1	19980107	EP 1996-911230	19960307
EP 815124	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1183102	A	19980527	CN 1996-193619	19960307
JP 11501920	T2	19990216	JP 1996-527647	19960307
BR 9607625	A	19990615	BR 1996-7625	19960307
RU 2174519	C2	20011010	RU 1997-116523	19960307
AT 229033	E	20021215	AT 1996-911230	19960307
PL 184771	B1	20021231	PL 1996-322179	19960307
PT 815124	T	20030430	PT 1996-911230	19960307
ES 2190793	T3	20030816	ES 1996-911230	19960307
CN 1530372	A	20040922	CN 2004-10039693	19960307

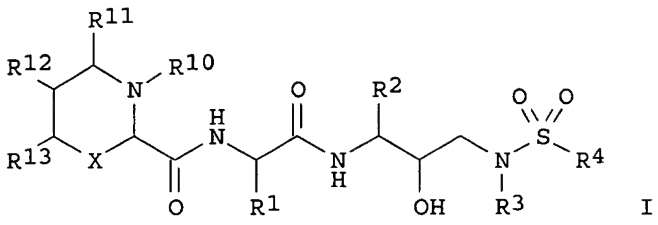
NO 9704147	A	19971104	NO 1997-4147	19970909
US 5972989	A	19991026	US 1998-28272	19980224
US 6063795	A	20000516	US 1999-307711	19990510
US 6214861	B1	20010410	US 2000-501265	20000209
US 6407134	B1	20020618	US 2001-775682	20010205
US 2003130202	A1	20030710	US 2002-120791	20020412
US 6673822	B2	20040106		
US 2004198989	A1	20041007	US 2003-715852	20031119

PRIORITY APPLN. INFO.:

US 1995-402419	B2 19950310
US 1995-392305	B2 19950410
US 1995-474117	A 19950607
WO 1996-US2683	W 19960307
US 1998-28272	A1 19980224
US 1999-307711	A1 19990510
US 2000-501265	A1 20000209
US 2001-775682	A1 20010205
US 2002-120791	A1 20020412

OTHER SOURCE(S): MARPAT 129:122867

GI



I

AB Heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide compds. I (X = bond or CH2; R1 = H, alkyl, alkenyl, alkynyl, imidazolylmethyl, CH2CONH2, CH2SO2NH2, etc.; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl, etc.; R10 = H, alkyl, benzyl, phenylmethoxycarbonyl, tert-butoxycarbonyl, 4-methoxyphenylmethoxycarbonyl; R11 = H, hydroxyalkyl, alkoxyalkyl; R12, R13 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, alkoxyalkyl; or R11 and R12 or R12 and R13 are optionally substituted benzo radical) were prepared as retroviral protease inhibitors. Thus, 2S-[[(pyrrolidin-2-yl)carbonyl]amino]-N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-3,3-dimethylbutanamide was assayed for protease inhibitory activity (IC50 = 2 nM, EC50 = 12 nM).

IT **143225-04-1P**

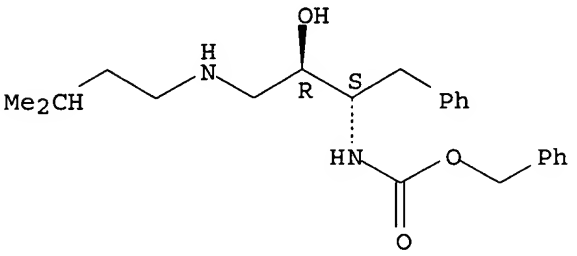
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:392091 CAPLUS

DOCUMENT NUMBER: 129:41411

TITLE: Preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors

INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 93 pp., Cont.-in-part of U. S. Ser. No. 402,287, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

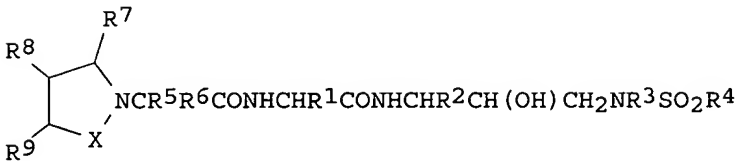
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756533	A	19980526	US 1995-474052	19950607
CA 2215061	AA	19960919	CA 1996-2215061	19960307
WO 9628463	A1	19960919	WO 1996-US2684	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9650294	A1	19961002	AU 1996-50294	19960307
AU 705268	B2	19990520		
EP 813542	A1	19971229	EP 1996-907135	19960307
EP 813542	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1186499	A	19980701	CN 1996-193620	19960307
JP 2001513746	T2	20010904	JP 1996-527648	19960307

AT 226213	E	20021115	AT 1996-907135	19960307
EP 1258491	A1	20021120	EP 2002-11526	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
PL 184748	B1	20021231	PL 1996-322784	19960307
PT 813542	T	20030131	PT 1996-907135	19960307
ES 2187640	T3	20030616	ES 1996-907135	19960307
EE 4349	B1	20040816	EE 1997-201	19960307
NO 9704148	A	19971027	NO 1997-4148	19970909
US 5965601	A	19991012	US 1998-33897	19980303
US 6140505	A	20001031	US 1998-80928	19980519
US 6310080	B1	20011030	US 1999-451920	19991201
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		
US 2003216435	A1	20031120	US 2002-200589	20020723
US 6730669	B2	20040504		
US 2004260095	A1	20041223	US 2004-760125	20040120

PRIORITY APPLN. INFO.:	US 1995-402287	B2 19950310
	US 1995-391873	B2 19950222
	US 1995-474052	A 19950607
	EP 1996-907135	A3 19960307
	WO 1996-US2684	W 19960307
	US 1998-80928	A1 19980519
	US 1999-451920	A3 19991201
	US 2001-836443	A1 20010418
	US 2002-200589	A1 20020723

OTHER SOURCE(S): MARPAT 129:41411

GI



I

AB Amino acid hydroxyethylamino sulfonamide compds. I (X = CH2 or CH2CH2; R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SMe, CMe2SMe or their sulfone or sulfoxide derivative; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl; R5 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R6 = H, alkyl, hydroxyalkyl, alkoxyalkyl, benzyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2CH2SMe, CH2SMe or their sulfone or sulfoxide derivs.; R7 = H, hydroxyalkyl, alkoxyalkyl; R8, R9 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, alkoxyalkyl; or R7 and R8 or R8 and R9 form a heteroaryl or benzo radical) were prepared as retroviral protease inhibitors.

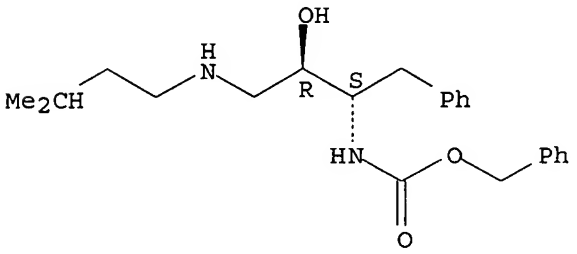
Thus, 2S-[(pyrrolidin-1-yl)acetylamino]-N-[2R-hydroxy-3-[N1-(2-methylpropyl)-N1-(2,3-dihydrobenzofuran-5-ylsulfonyl)amino]-1S-(phenylmethyl)propyl]-3S-methylpentanamide, prepared from N-[3S-benzyloxycarbonylamino-2R-hydroxy-4-phenylbutyl]-N-isobutylamine, tert-Bu bromoacetate, pyrrolidine, and 2,3-dihydrofuran, showed HIV protease inhibitory activity IC50 = 2 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:392089 CAPLUS
DOCUMENT NUMBER: 129:40987
TITLE: Sulfonylalkanoylamino hydroxyethylamino sulfonyl urea derivatives useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Sun, Eric T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 29 pp., Cont. of U. S. Ser. No. 969,616, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756498	A	19980526	US 1996-589563	19960111
PRIORITY APPLN. INFO.:			US 1992-969616	B1 19921030

OTHER SOURCE(S): MARPAT 129:40987

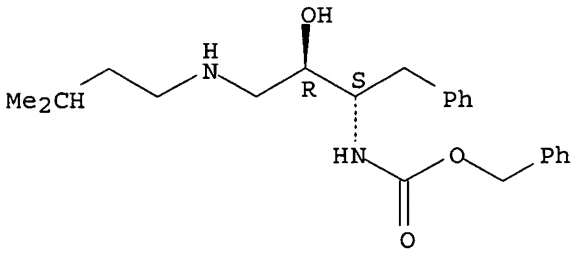
AB Sulfonylalkanoylamino hydroxyethylamino sulfonyl urea derivs. RSOx(CH2)tCR20R21CHR1C(Y)NR6CHR2CH(OH)CH2NR3SOxNR4CR7R7'(CH2)nR8 [R = alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R1 R20, R21 = H, CH2SO2NH2, CH2CO2Me, haloalkyl, etc.; R2 = alkyl, aryl, cycloalkyl, etc.; R3 =

alkyl, haloalkyl, alkenyl, alkynyl, etc.; R4 = H, radicals as defined for R3; R6 = H, alkyl; R7, R7' = H, amino acid side chains, etc.; R8 = cyano, OH, alkyl, alkoxy, etc.; x = 1, 2; t = 0-2; n = 0-6; Y = S, S, NR15], effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease (no data), were prepared E.g., N-[[[2R-hydroxy-3S-[[2S-methyl-3-(methylsulfonyl)-1-oxopropyl]amino]-4-phenylbutyl](3-methylbutyl)amino]sulfonyl]-2-methylalanine Et ester was prepared

IT **143225-04-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonyl urea derivs. useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:331371 CAPLUS
DOCUMENT NUMBER: 129:16395
TITLE: Preparation of phenylstatine derivatives as retroviral protease inhibitors
INVENTOR(S): Chang, Min S.; Getman, Daniel P.; Mueller, Richard A.; Ottinger, James C.; Stolzenbach, James C.; Talley, John J.; Vazquez, Michael L.; Decrescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 109,787, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5750648	A	19980512	US 1994-253531	19940603
WO 9506061	A1	19950302	WO 1994-US8697	19940809

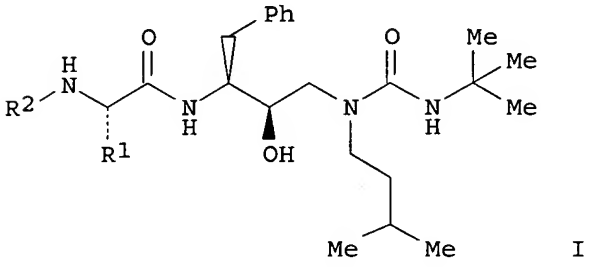
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG,

MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT,
UA, US, UZ, VN
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
SN, TD, TG

AU 9475186	A1	19950321	AU 1994-75186		19940809
ZA 9406325	A	19950821	ZA 1994-6325		19940819
IL 110724	A1	19990817	IL 1994-110724		19940819
PRIORITY APPLN. INFO.:			US 1993-109787	B2	19930820
			US 1994-253531	A	19940603
			WO 1994-US8697	W	19940809

OTHER SOURCE(S): MARPAT 129:16395

GI



I

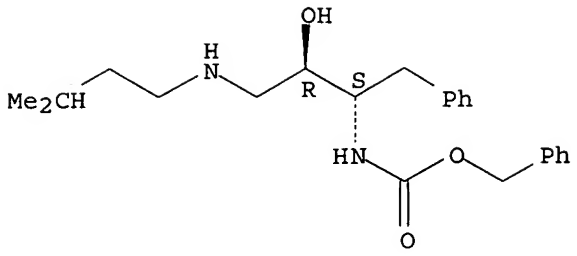
AB The present invention is directed to the preparation and use of retroviral protease inhibitors I [R1 = CHMe2, CHMeEt, CMe3, CMe2SMe, CMe2S(O)Me, CMe2SO2Me; R2 = Me-L-Ala, Me-D-Ala, H-Gly, Me-Gly, H-L-Pro, H-D-Pro, H-L-Ile each optionally substituted on the nitrogen atom with benzyloxycarbonyl or tert-butoxycarbonyl], or a pharmaceutically acceptable salt or ester thereof, and combinations of retroviral protease inhibitors which are effective in preventing the replication of mammalian retroviruses, such as human immunodeficiency virus (HIV). Thus, coupling of N-benzyloxycarbonyl-N-methyl-L-alanine with reduced peptide mimic I (R1 = CMe3; R2 = H) (prepared in 7 steps from N-benzyloxycarbonyl-L-phenylalanine chloromethyl ketone, isoamylamine, tert-Bu isocyanate, and N-benzyloxycarbonyl-L-tert-butylglycine), followed by catalytic deprotection, gave 54% desired inhibitor I (R1 = CMe3, R2 = Me-L-Ala) (II). II inhibited HIV-infected cells with IC50 = 8 nM, and EC50 = 96 mg/mL in the presence of AZT or DDI.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylstatine derivs. as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

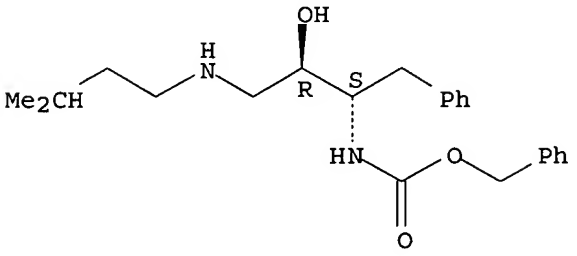
L3 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:324825 CAPLUS
DOCUMENT NUMBER: 129:16390
TITLE: Preparation of substituted sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Sikorski, James A.; Getman, Daniel P.; Decrescenzo, Gary A.; Devadas, Balekudru; Freskos, John N.; Lu, Hwang-fun; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 131 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5753660	A	19980519	US 1996-747357	19961113
PRIORITY APPLN. INFO.:			US 1996-747357	19961113

OTHER SOURCE(S): MARPAT 129:16390
AB Sulfonylalkanoylamino hydroxyethylamino sulfonamides R5S(O)m(CH2)nCHR1C(:W)NHCHR2CH(OH)CH2NR1SO2R4 (W = O, S; m, n = 0, 1, or 2; R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, NH2COCH2, NH2COCH2CH2, NH2SO2CH2, MeSCH2, MeSOCH2, MeSO2CH2; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylalkyl; R4 = aryl, heteroaryl, heterocyclyl; R5 = heteroaryl, heterocyclyl) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-[2-(2-pyridyl)ethylsulfonyl]propanamide was prepared by alkylation of the corresponding 3-mercaptopropanamide with 2-(2-chloroethyl)pyridine hydrochloride, followed by S-oxidation The product was assayed for HIV protease inhibitory activity (IC50 = 3 nM, EC50 = 6 nM).
IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)
RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-

(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:41716 CAPLUS
DOCUMENT NUMBER: 128:115228
TITLE: Preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Mcdonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 401,838, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5705500	A	19980106	US 1995-478625	19950607
CA 2215066	AA	19960919	CA 1996-2215066	19960307
CA 2215066	C	20060606		
WO 9628418	A1	19960919	WO 1996-US2682	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9666951	A1	19961002	AU 1996-66951	19960307
AU 711098	B2	19991007		
EP 813519	A1	19971229	EP 1996-911229	19960307
EP 813519	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1183767	A	19980603	CN 1996-193609	19960307
BR 9607450	A	19980630	BR 1996-7450	19960307
JP 11503414	T2	19990326	JP 1996-527646	19960307
EP 1052250	A1	20001115	EP 2000-114155	19960307

EP 1052250	B1	20040714			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
AT 201014	E	20010515	AT 1996-911229		19960307
ES 2157437	T3	20010816	ES 1996-911229		19960307
PT 813519	T	20011031	PT 1996-911229		19960307
SK 282893	B6	20030109	SK 1997-1223		19960307
PL 186059	B1	20030930	PL 1996-322169		19960307
AT 271034	E	20040715	AT 2000-114155		19960307
EE 4340	B1	20040816	EE 1997-199		19960307
PT 1052250	T	20041130	PT 2000-114155		19960307
ES 2226665	T3	20050401	ES 2000-114155		19960307
NO 9704146	A	19971107	NO 1997-4146		19970909
NO 310353	B1	20010625			
GR 3036254	T3	20011031	GR 2001-401103		20010724
PRIORITY APPLN. INFO.:			US 1995-401838	B2	19950310
			US 1995-478625	A	19950607
			EP 1996-911229	A3	19960307
			WO 1996-US2682	W	19960307

OTHER SOURCE(S): MARPAT 128:115228

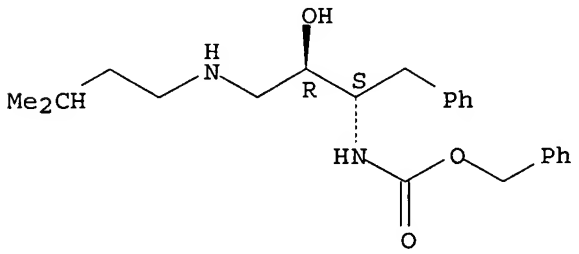
AB Sulfonylalkanoylamino hydroxyethylamino sulfonamide compds. R5S(O)t(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2SOMe, CH2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = benzo-fused heteroaryl or heterocyclyl; n, t = 0-2) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-(methylsulfonyl)propanamide was prepared and assayed for HIV protease inhibitory activity (IC50 = 2 nM; EC50 = 20 nM).

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

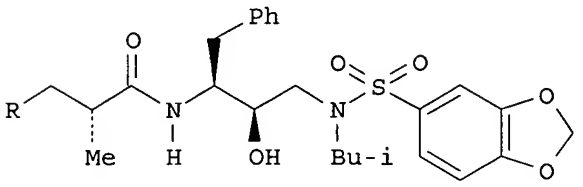


REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:450087 CAPLUS
DOCUMENT NUMBER: 127:65754
TITLE: Preparation of N-[2-hydroxy-4-phenyl-3-(sulfonylalkanoylamino)butyl]arylsulfonamides and analogs as retroviral protease inhibitors
INVENTOR(S): Sikorski, James A.; Getman, Daniel P.; Decrescenzo, Gary A.; Devadas, Balekudru; Freskos, John N.; Lu, Hwang-fun; Mcdonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Sikorski, James A.; Getman, Daniel P.; Decrescenzo, Gary A.; Devadas, Balekudru; Freskos, John N.; Lu, Hwang-Fun; Mcdonald, Joseph J.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718205	A1	19970522	WO 1996-US17771	19961113
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2236236	AA	19970522	CA 1996-2236236	19961113
AU 9677222	A1	19970605	AU 1996-77222	19961113
EP 861249	A1	19980902	EP 1996-940302	19961113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000515488	T2	20001121	JP 1997-518913	19961113
PRIORITY APPLN. INFO.:			US 1995-6767P P	19951115
			WO 1996-US17771 W	19961113

OTHER SOURCE(S): MARPAT 127:65754
GI



II

AB R5SOt(CH2)nC(:W)NHCHR2CH(OH)CH2NR3SO2R4 [I; R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = (ar)alkyl, alkylthioalkyl, arylthioalkyl,

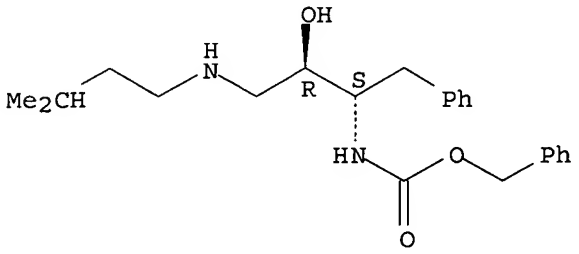
etc.; R3 = (cyclo)alkyl, cycloalkylalkyl, etc.; R5 = heterocyclyl(alkyl), (hetero)aryl(alkyl), etc.; W = O or S; n,t = 0-2] were prepared Thus, (2R,3S)-PhCH2O2CNHCH(CH2Ph)CH(OH)CH2NHCH2CHMe2 (preparation given) was amidated by benzodioxole-5-sulfonyl chloride and the deprotected product amidated by (S)-AcSCH2CHMeCO2H to give, after deprotection, sulfonamide II (R = SH). The latter was S-alkylated by 2-(2-chloroethyl)pyridine (preparation given) and the product oxidized to give II [R = 2-(2-pyridyl)ethylsulfonyl]. Data for biol. activity of I were given.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-[2-hydroxy-4-phenyl-3-(sulfonylalkanoylamino)butyl]arylsulfonamides and analogs as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1997:8904 CAPLUS
DOCUMENT NUMBER:	126:31657
TITLE:	Preparation of N-heterocyclecarbonyl amino acid hydroxyethylamino sulfonamide as retroviral protease inhibitors
INVENTOR(S):	Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; Mcdonald, Joseph J.
PATENT ASSIGNEE(S):	G.D. Searle and Co., USA
SOURCE:	PCT Int. Appl., 184 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

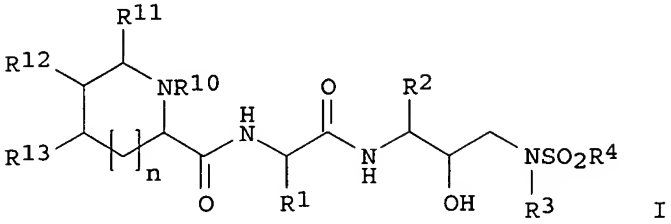
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628465	A1	19960919	WO 1996-US2683	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5776971	A	19980707	US 1995-474117	19950607

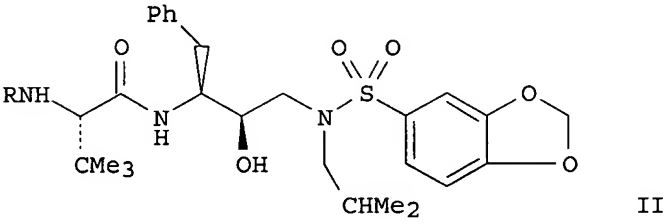
AU 9654178	A1	19961002	AU 1996-54178	19960307
AU 717598	B2	20000330		
EP 815124	A1	19980107	EP 1996-911230	19960307
EP 815124	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11501920	T2	19990216	JP 1996-527647	19960307
BR 9607625	A	19990615	BR 1996-7625	19960307
RU 2174519	C2	20011010	RU 1997-116523	19960307
AT 229033	E	20021215	AT 1996-911230	19960307
PL 184771	B1	20021231	PL 1996-322179	19960307
NO 9704147	A	19971104	NO 1997-4147	19970909
US 6172101	B1	20010109	US 1998-894984	19980423
PRIORITY APPLN. INFO.:			US 1995-402419	A2 19950310
			US 1995-474117	A2 19950607
			WO 1996-US2683	W 19960307

OTHER SOURCE(S): MARPAT 126:31657

GI



I



II

AB Selected heterocyclecarbonyl amino acid hydroxyethylamino sulfonamide compds. of formula [I; R1 = C1-5 alkyl, C2-5 alkenyl or alkynyl, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, cyano-C1-3 alkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2(S)nNH2 (n = 0, 1,2), CMe2(S)nMe (n = 0,1,2); R2 = C1-5 alkyl, C1-3 alkyl, alkylthio-C1-3 alkyl, arylthio-C1-3 alkyl, 3- to 6-membered cycloalkyl-C1-3 alkyl; R4 = aryl, benzo-fused 5- to 6-membered heteroaryl or heterocyclyl, etc.; R10 = H, C1-3 hydroxyalkyl, alkoxy-C1-3 alkyl; R12, R13 = H, OH, HOCH2CH2, C1-3 hydroxyalkyl, alkoxy-C1-3 alkyl; or R11 and R12 or R12 and R13 along with the C atoms to which they are attached represent a benzo radical optionally substituted with at least one HO or C1-3 alkoxy radical] are effective as retroviral protease inhibitors, and in particular as inhibitor of HIV protease, and for the treatment of AIDS. The present invention relates to such retroviral protease inhibitors and, more particularly, relates to selected novel compds., composition and method for inhibiting retroviral proteases, such as human immunodeficiency virus (HIV) protease, prophylactically preventing

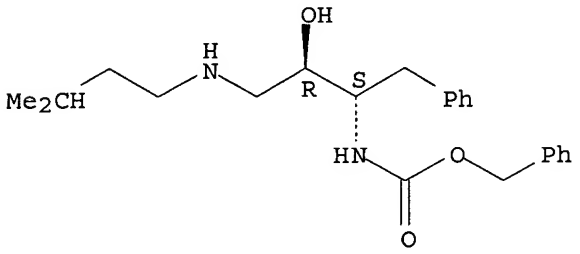
retroviral infection or the spread of a retrovirus, and the treatment of a retroviral infection. Thus, tert-leucine derivative (II; R = H) (preparation given) was condensed with Z-Pro-OH using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and HOBt in DMF followed by hydrogenolysis and acidification with HCl to give proline-containing peptide analog II.HCl (R = H-Pro). The latter compound in vitro showed IC50 of 1 nM for inhibiting the proliferation of HIV-1 in CEM cells.

IT **143225-04-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-heterocyclecarbonyl amino acid N-[hydroxy(sulfonamido)propyl]amides as retroviral protease inhibitors for AIDS treatment)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:725344 CAPLUS

DOCUMENT NUMBER: 126:75247

TITLE: Preparation of α- and β-amino acid hydroxyethylamino sulfonyl urea derivatives as retroviral protease inhibitors

INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Sun, Eric T.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 37 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

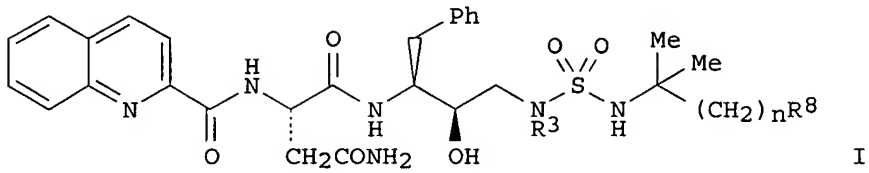
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

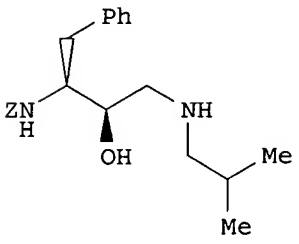
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5578606	A	19961126	US 1992-968712	19921030
US 6022872	A	20000208	US 1996-709069	19960906
US 6211176	B1	20010403	US 1999-345739	19990701
US 6403585	B1	20020611	US 2000-731911	20001208
US 2003144342	A1	20030731	US 2002-138534	20020506
US 6683648	B2	20040127		
US 2004171653	A1	20040902	US 2003-689513	20031021
US 7030161	B2	20060418		
US 2006094789	A1	20060504	US 2005-235524	20050927
PRIORITY APPLN. INFO.:			US 1992-968712	A3 19921030

US 1996-709069	A1	19960906
US 1999-345739	A1	19990701
US 2000-731911	A1	20001208
US 2002-138534	A1	20020506
US 2003-689513	A1	20031021

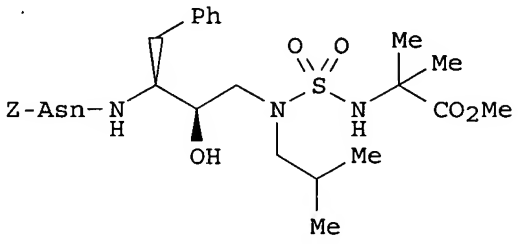
OTHER SOURCE(S): MARPAT 126:75247
GI



I



II



III

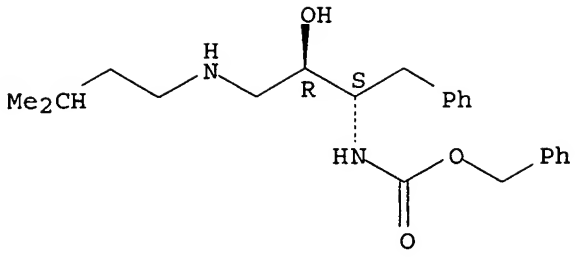
AB α- And β-amino acid hydroxyethylamino sulfonyl urea derivative compds., e.g. I [R3 = C1-8 alkyl, (un)substituted C1-8 alkylphenyl, C1-8 heteroaralkyl; R8 = (un)substituted Ph, heterocyclyl, CN, OH, CO2H, C1-8 alkylthio, (un)substituted phenylsulfonyl, C1-8 alkanoyl, C1-8 alkoxycarbonyl, C1-8 dialkylaminocarbonyl, N-C1-8-alkyl-N-phenylcarbamoyl, 2-heterocyclylethoxy, heterocyclyl; n = 0-2], are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease. Thus, coupling of protected amino(hydroxy)phenylbutylamine II (Z = PhCH2O2C) (prepared in 3 steps from chloromethyl ketone Z-L-Phe-CH2Cl) with ClSO2NHCMe2CO2Me, followed by hydrogenolysis and coupling with Z-Asn-OH gave inhibitor III.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hydroxyethylamino sulfonyl urea peptide derivs. as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:667025 CAPLUS
DOCUMENT NUMBER: 125:328302
TITLE: Preparation of N-[[(sulfonylalkanoyl)amino]hydroxy alkyl]sulfonamides as retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628418	A1	19960919	WO 1996-US2682	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5705500	A	19980106	US 1995-478625	19950607
CA 2215066	AA	19960919	CA 1996-2215066	19960307
CA 2215066	C	20060606		
AU 9666951	A1	19961002	AU 1996-66951	19960307
AU 711098	B2	19991007		
EP 813519	A1	19971229	EP 1996-911229	19960307
EP 813519	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
BR 9607450	A	19980630	BR 1996-7450	19960307
JP 11503414	T2	19990326	JP 1996-527646	19960307
AT 201014	E	20010515	AT 1996-911229	19960307
SK 282893	B6	20030109	SK 1997-1223	19960307
PL 186059	B1	20030930	PL 1996-322169	19960307
EE 4340	B1	20040816	EE 1997-199	19960307
NO 9704146	A	19971107	NO 1997-4146	19970909
NO 310353	B1	20010625		
US 5985870	A	19991116	US 1997-913069	19971219
US 6380188	B1	20020430	US 2000-672449	20000929
GR 3036254	T3	20011031	GR 2001-401103	20010724

US 2003191166	A1	20031009	US 2002-82123	20020226
US 6667307	B2	20031223		
US 2004147758	A1	20040729	US 2003-677729	20031003
US 7045518	B2	20060516		
PRIORITY APPLN. INFO.:			US 1995-401838	A2 19950310
			US 1995-478625	A2 19950607
			WO 1996-US2682	W 19960307
			US 1997-913069	A1 19971219
			US 1999-411374	A1 19991004
			US 2000-672449	A1 20000929
			US 2002-82123	A1 20020226

OTHER SOURCE(S): MARPAT 125:328302

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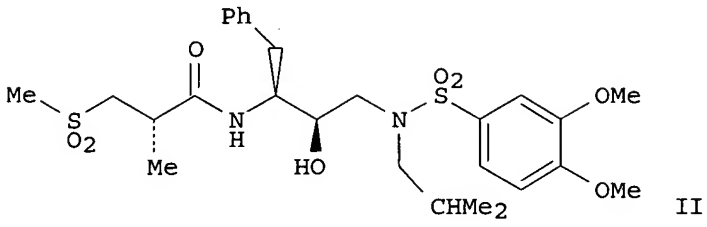


II

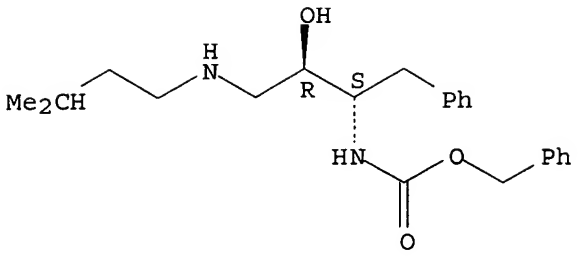
AB R5SOm(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 [I; R1 = H, (hydroxy)alkyl, CH2CONH2, etc.; R2 = (ar)alkyl, alkylthioalkyl, etc.; R3 = (cyclo)alkyl, cycloalkylmethyl; R4 = heterocyclyl, heteroaryl, etc.; R5 = (ar)alkyl, alkenyl, alkynyl; m,n = 0-2] were prepared Thus, (2S,3S)-N-benzyloxycarbonyl-3-amino-1,2-epoxy-4-phenylbutane (preparation given) was condensed with Me2CHCH2NH2 and the product amidated by 3,4-(MeO)C6H3SO2Cl to give, after deprotection and (S)-MeSO2CH2CHMeCO2H amidation, title compound II. Data for activity of selected I in an in vitro HIV inhibition assay were given.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-[[(sulfonylalkanoyl)amino]hydroxyalkyl]sulfonamides as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:572053 CAPLUS
DOCUMENT NUMBER: 125:222459
TITLE: Preparation of bis(sulfonamido hydroxyethylamino peptide analogs as retroviral protease inhibitors.
INVENTOR(S): Freskos, John N.; Getman, Daniel P.; Talley, John J.; Sikorski, James A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

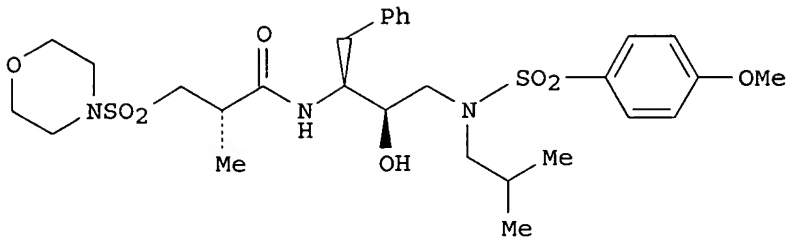
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622287	A1	19960725	WO 1996-US607	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
CA 2210889	AA	19960725	CA 1996-2210889	19960118
AU 9647008	A1	19960807	AU 1996-47008	19960118
EP 804428	A1	19971105	EP 1996-902700	19960118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 11500105	T2	19990106	JP 1996-522362	19960118
EP 1586558	A2	20051019	EP 2005-13695	19960118
EP 1586558	A3	20051026		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 6143747	A	20001107	US 1998-875025	19980226
US 6384036	B1	20020507	US 2000-635896	20000811
US 2003013751	A1	20030116	US 2002-76607	20020219
US 2004063771	A1	20040401	US 2003-417340	20030417

PRIORITY APPLN. INFO.:

US 1995-376337	A	19950120
EP 1996-902700	A3	19960118
WO 1996-US607	W	19960118
US 1998-875025	A1	19980226
US 2000-635896	A1	20000811

US 2002-76607 A1 20020219

OTHER SOURCE(S): MARPAT 125:222459
GI



I

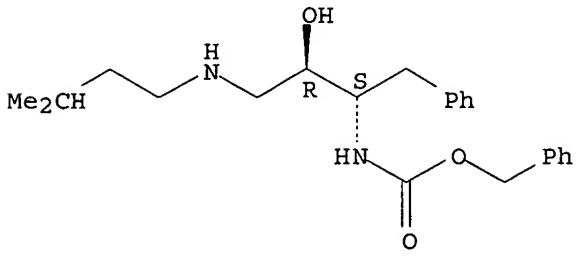
AB R10R11NSOw(CR7R8)tCHR1C(:Y)NR6CHR2CH(OH)CH2NR3SOxR4 [R1 = H, CH2SO2NH2, CH2SO2Me, CO2Me CONH2, alkyl, haloalkyl, heterocycloalkyl, amino acid side chain (derivative), etc.; R2 = halo, NO2, cyano, CF3, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, etc.; R3 = alkyl, alkenyl, alkynyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkylsulfinylalkyl, alkylthioalkyl, arylthioalkyl, heteroaryl, etc.; R4 = alkyl, alkenyl, alkynyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryl, aralkyl, thioalkyl, heteroaryl, heterocycloalkyl, etc.; R6, R8 = H, alkyl; R7 = CO2H, amidino, R1; R1R7 = atoms to form a cycloalkyl or heterocyclyl ring; R10, R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, heterocycloalkyl, aryl, aralkyl, heteroaryl, thioalkyl, alkylthioalkyl, etc.; R10R11N = heterocyclo, aralkylheterocyclo, heteroaryl, etc.; x, w = 0-2; t = 0-6; Y = O, S, NH], were prepared Thus, 3-(4-morpholinosulfonyl)-2(R)-methylpropionic acid (preparation given) in DMF was treated with hydroxybenzotriazole, EDC, and 3(S)-amino-1-[N-(2-methylpropyl)-N-(4-methoxyphenylsulfonyl)amino]-4-phenyl-2(R)-butanol (preparation given) to give title compound (I). I inhibited HIV protease with IC50 = 10 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(sulfonamido hydroxyethylamino peptide analogs as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

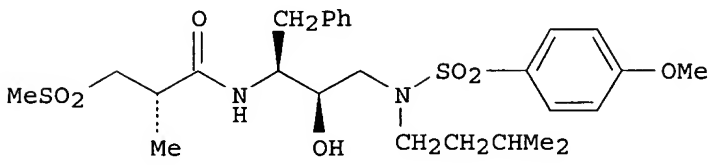


L3 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:380218 CAPLUS
DOCUMENT NUMBER: 125:142289
TITLE: Sulfonylalkanoylamino hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 935,071, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5521219	A	19960528	US 1993-110913	19930824
AT 161828	E	19980115	AT 1993-920214	19930824
ES 2112430	T3	19980401	ES 1993-920214	19930824
FI 9500651	A	19950214	FI 1995-651	19950214
US 5508294	A	19960416	US 1995-455051	19950531
US 5510388	A	19960423	US 1995-455947	19950531
US 5639769	A	19970617	US 1996-587688	19960117
US 5760064	A	19980602	US 1997-867430	19970606
US 5965588	A	19991012	US 1998-48034	19980326
US 6147117	A	20001114	US 1999-352215	19990713
US 6743929	B1	20040601	US 2000-655844	20000906
US 2004267022	A1	20041230	US 2004-750213	20040102

PRIORITY APPLN. INFO.: US 1992-935071 B2 19920825
US 1993-110913 A3 19930824
US 1996-587688 A1 19960117
US 1997-867430 A1 19970606
US 1998-48034 A1 19980326
US 1999-352215 A1 19990713
US 2000-655844 A3 20000906

OTHER SOURCE(S): MARPAT 125:142289
GI



I

AB RSO2(CH2)tCH2CHR1C(:Y)NHCHR2CH(OH)CH2NR3SO2R4 (R = alkyl, alkenyl,

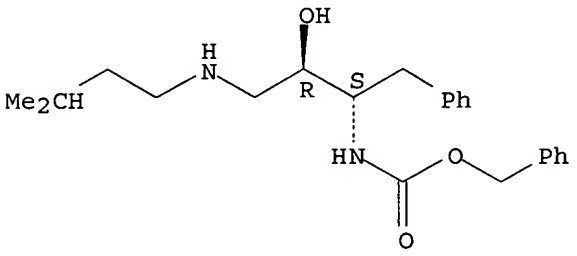
aryl, etc.; R1 = H, CMe2SMe, alkyl, haloalkyl, amino acid side chain, etc.; R2 = alkyl, aryl, cycloalkyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; R4 = alkyl, cycloalkyl, aryl, etc.; t = 0, 1; Y = O, S) and their salts were prepared as retroviral protease inhibitors. Thus, I was prepared in several steps and shown to have an IC50 of 3.2 nanomolar when tested against HIV protease.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(sulfonylalkanoylamino hydroxyethylamino sulfonamides as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:35006 CAPLUS

DOCUMENT NUMBER: 124:261768

TITLE: Urea-containing hydroxyethylamine peptides as retroviral protease inhibitors

INVENTOR(S): Talley, John J.; Getman, Daniel P.; Freskos, John N.; Lin, Ko-chung; Heintz, Robert M.; Rogier, Jr Donald J.; Bertenshaw, Deborah E.

PATENT ASSIGNEE(S): Monsanto Co., USA

SOURCE: U.S., 60 pp. Cont.-in-part of U.S. Ser. No. 789,642, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5475013	A	19951212	US 1992-886531	19920520
EP 731088	A2	19960911	EP 1996-107359	19911118
EP 731088	A3	19970514		
EP 731088	B1	20001004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 735019	A2	19961002	EP 1996-107357	19911118
EP 735019	A3	19970514		
EP 735019	B1	20000920		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 813867	A2	19971229	EP 1997-105350	19911118
EP 813867	A3	19980401		
EP 813867	B1	20050601		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 813868	A2	19971229	EP 1997-105352		19911118
EP 813868	A3	19980318			
EP 813868	B1	20050601			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 815856	A2	19980107	EP 1997-105351		19911118
EP 815856	A3	19980318			
EP 815856	B1	20050601			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5475027	A	19951212	US 1993-148817		19931108
US 5510378	A	19960423	US 1995-449974		19950525
US 5510487	A	19960423	US 1995-452603		19950525
US 5602175	A	19970211	US 1995-450606		19950525
US 5648511	A	19970715	US 1995-452187		19950525
US 5703076	A	19971230	US 1995-449966		19950525
US 5708004	A	19980113	US 1995-450605		19950525
US 5510349	A	19960423	US 1995-471898		19950607
US 5610190	A	19970311	US 1995-476009		19950607
US 5620977	A	19970415	US 1995-474569		19950607
US 5622949	A	19970422	US 1995-476010		19950607
US 5698569	A	19971216	US 1995-487664		19950607
US 5614522	A	19970325	US 1995-506213		19950724
US 5872298	A	19990216	US 1997-833737		19970409
US 5872299	A	19990216	US 1997-854133		19970508
GR 3034894	T3	20010228	GR 2000-402583		20001122
GR 3035176	T3	20010430	GR 2000-402865		20001229
PRIORITY APPLN. INFO.:			US 1990-615210	B2	19901119
			US 1991-789642	B2	19911220
			US 1991-789643	A	19911114
			US 1991-789644	B2	19911114
			US 1991-789645	B2	19911114
			US 1991-789646	B2	19911114
			EP 1992-901068	A3	19911118
			EP 1992-901691	A3	19911118
			US 1992-886531	A3	19920520
			US 1992-886547	B1	19920520
			US 1992-886556	B1	19920520
			US 1992-886558	B2	19920520
			US 1992-886663	B3	19920520
			US 1993-148817	A3	19931108
			US 1993-152934	A3	19931115
			US 1993-156498	B3	19931123
			US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 124:261768
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

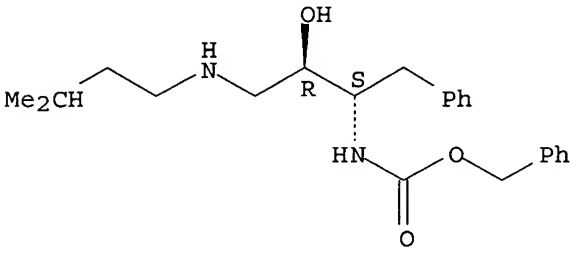
AB Urea-containing peptide compds. I or their pharmaceutically acceptable salts, prodrugs, or esters thereof, wherein: A = radical represented by the formulas II, RR'N(CR1'R1'')qCHR1C(:Y'), III; R = e.g., H, alkoxycarbonyl, aralkoxycarbonyl; R' = e.g., H and radicals as defined for R3; q = 0, 1; R1 = e.g., H, CH2SO2NH2, CO2Me, amino acid side chains; R1', R1'' = e.g., H and radicals defined for R1; R2 = e.g., alkyl, aryl, cycloalkyl; R3 = e.g., alkyl, alkenyl, alkynyl; X' = e.g., O, CR17 where R17 = H, alkyl, and N; Y, Y', Y'' = O, S, NR15 wherein R15 = H and radicals as defined for R3; B = CR7R7'(CH2)nR8; n = 0-6; R7 and R7' = e.g., radicals as defined for R3 and amino acid side chains; R8 = e.g., CN, OH, alkyl, alkoxy; R4 = H and radicals defined by R3; R6 = H, alkyl; R20, R21, R30, R31, R32 = e.g., radicals as defined for R1; R33, R34 = e.g., H, radicals as defined for R3; are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease. Thus, e.g., Curtius rearrangement of 2,2-dimethyl-3-(4-pyridyl)propionic (preparation given) with diphenylphosphoryl azide, followed by coupling with 3(S)-[N-(2-quinolinylcarbonyl)-L-asparaginyl]amino-2(R)-hydroxy-4-phenylbutyl-N-(4-fluorophenylmethyl)amine afforded butanediamide, N1-[3-[[[(1,1-dimethyl-2-(4-pyridyl)ethyl)amino]carbonyl](4-fluorophenylmethyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(2-quinolinylcarbonyl)amino]-, [1S-[1R*(R*),2S*]] (IV) which inhibited HIV protease with IC50 = 4 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(urea-containing hydroxyethylamine peptides as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



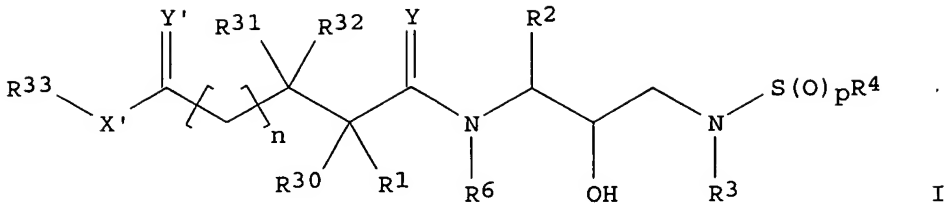
L3 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:964989 CAPLUS
DOCUMENT NUMBER: 124:176937
TITLE: N-[(Succinoylamino)hydroxypropyl]sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley,

	John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S):	G. D. Searle and Co., USA
SOURCE:	U.S., 32 pp. Cont.-in-part of U.S. Ser. No. 935,490, abandoned CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5463104	A	19951031	US 1993-110912	19930824
AT 154800	E	19970715	AT 1993-920213	19930824
ES 2103488	T3	19970916	ES 1993-920213	19930824
US 5714605	A	19980203	US 1995-541350	19951010
US 5760076	A	19980602	US 1995-541747	19951010
US 6022994	A	20000208	US 1998-41016	19980312
US 6313345	B1	20011106	US 1999-419816	19991018
US 2002137942	A1	20020926	US 2001-884462	20010620
US 6469207	B2	20021022		
US 2003220508	A1	20031127	US 2002-237184	20020909
US 6727282	B2	20040427		
US 2005004043	A1	20050106	US 2004-784916	20040224
US 7038084	B2	20060502		

PRIORITY APPLN. INFO.:	US 1992-935490	B2	19920825
	US 1993-110912	A3	19930824
	US 1995-541350	A1	19951010
	US 1995-541747	A1	19951010
	US 1998-41016	A1	19980312
	US 1999-419816	A1	19991018
	US 2001-884462	A1	20010620
	US 2002-237184	A1	20020909

OTHER SOURCE(S):	MARPAT 124:176937
GI	



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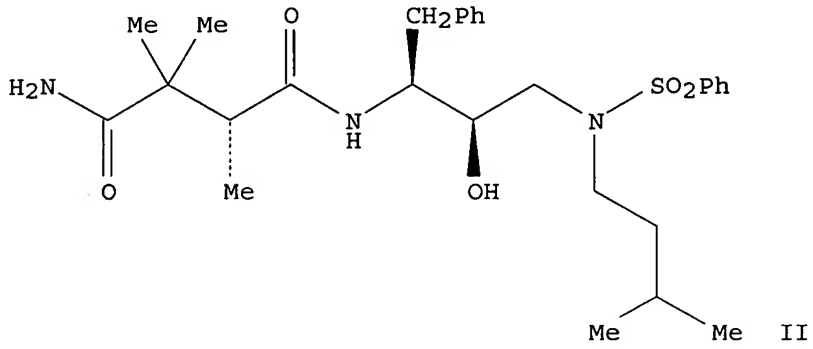


II

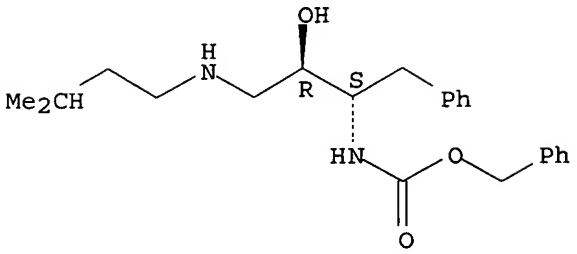
AB Succinoylamino hydroxyethylamino sulfonamide compds. I or a pharmaceutically acceptable salt or ester thereof, wherein p represents 0, 1 or 2; n represents either 0 or 1; X' represents N(R34) or O; or R33X' represents cycloalkyl or aryl radicals; Y and Y' each independently represent O or S; R1, R30, R31 and R32 each independently represent hydrogen, OH, (CH2)C(O)CH3, CH2SO2NH2, CO2CH3, CONHCH3, CON(CH3)2, CH2C(O)NHCH3, CH2C(O)N(CH3)2, CONH2, C(CH3)2(SH), C(CH3)2(SCH3), C(CH3)2[S(O)CH3], C(CH3)2[S(O)2CH3], alkyl, haloalkyl, alkenyl, alkynyl, aralkyl or cycloalkyl radicals, or the side chain of the amino acid asparagine, S-Me cysteine or the corresponding sulfoxide or sulfone derivs. thereof, leucine, isoleucine, allo-isoleucine, tert-leucine, phenylalanine, ornithine, alanine, norleucine, glutamine, valine, threonine, serine, o-alkyl serine, aspartic acid, β-cyanoalanine or allothreonine; or R30 and R32 together with the carbon atoms to which they are attached form a cycloalkyl radical; R2 = e.g., alkyl, aryl, cycloalkyl; R3, R33, R34 = e.g., H, alkyl, haloalkyl; R4 = e.g., alkyl, haloalkyl, alkenyl; R6 = H, alkyl; are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease. Thus, e.g., butanediamide II was prepared by coupling of benzyl (R)-2,2,3-trimethylsuccinate (preparation given) with 2(R)-hydroxy-3-[(3-methylbutyl)(phenylsulfonyl)amino]-1(S)-(phenylmethyl)propylamine (preparation given) followed by benzyl ester hydrogenolysis and amidation, and exhibited IC50 = 2 nM for inhibition of HIV protease.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(N-[(succinoylamino)hydroxypropyl]sulfonamides useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:871984 CAPLUS
DOCUMENT NUMBER: 123:279761
TITLE: Hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Bertenshaw, Deborah E.; Heintz, Robert M.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9506030	A1	19950302	WO 1994-US9139	19940823
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5843946	A	19981201	US 1993-110911	19930824
US 6060476	A	20000509	US 1994-204827	19940302
AU 9476697	A1	19950321	AU 1994-76697	19940823
EP 715618	A1	19960612	EP 1994-927162	19940823
EP 715618	B1	19981216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 6046190	A	20000404	US 1996-586866	19960124

PRIORITY APPLN. INFO.:		
US 1993-110911	A	19930824
US 1994-204827	A	19940302
US 1992-934984	B2	19920825
WO 1993-US7814	A2	19930824
US 1994-204872	B2	19940302
WO 1994-US9139	W	19940823

OTHER SOURCE(S): MARPAT 123:279761

AB Hyroxethylamino sulfonamide compds. AC(:Y)NR6CHR2CHOHCH2NR3S(:O)xR4 [I: R2=(substituted)alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R3=H; R3,R4=R2, alkenyl, alkynyl, heterocycloalkyl, -aryl, -aralkyl, -cycloalkyalkyl; R6=H, alkyl; x=1,2; Y=O, S; A=RO, R; R=alkyl, alkenyl; (hetero)aryl, cycloalkyl, cycloalkylalkyl, aralkyl, NH2, mono- or disubstituted amino, etc.] are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease. Many inhibitors were prepared by (1) preparing an N-protected amino epoxide and (2) reacting this with an amine and (3) preparing a sulfonamide by reacting with a sulfonyl chloride or sulfonyl anhydride in the presence of an acid scavenger. The amino function of the sulfonamide was then (4) deprotected and (5) reacted with a carboxylate. In vitro HIV protease assays with these compds. revealed inhibitors with IC50's as low as 1.4 nM, e.g. [1S-[1R*(S*),2S*]]-I (A=p-MeOC6H4CH2OCONHCH2CHMe; Y=O; R6=H; R2=benzyl; R3=3-methylbutyl; x=2; R4=phenyl).

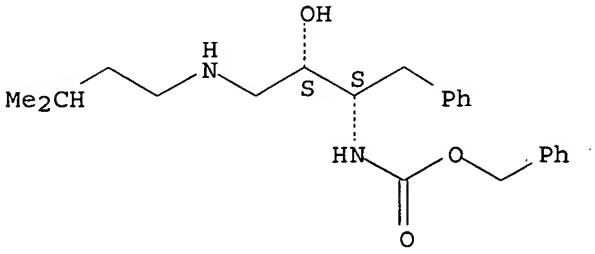
IT **159006-48-1**

RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 159006-48-1 CAPLUS

CN Carbamic acid, [(1S,2S)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



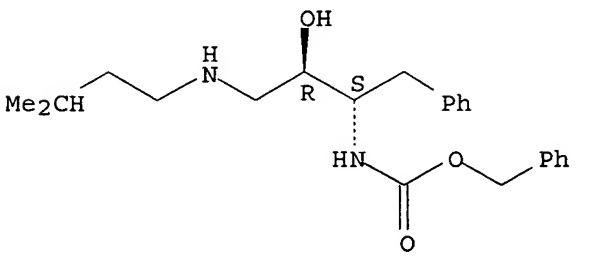
IT **143225-04-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

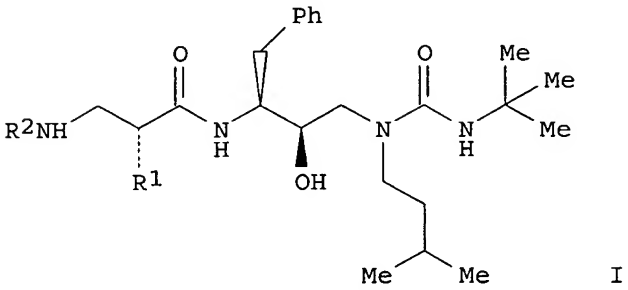


L3 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:807958 CAPLUS
DOCUMENT NUMBER: 123:228913
TITLE: Preparation of peptide analogs as retroviral protease inhibitors.
INVENTOR(S): Chang, Min S.; Stolzenbach, James C.; Talley, John J.; Vazquez, Michael L.; Getman, Daniel P.; Mueller, Richard A.; Ottinger, James C.; Decrescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9506061	A1	19950302	WO 1994-US8697	19940809
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5750648	A	19980512	US 1994-253531	19940603
AU 9475186	A1	19950321	AU 1994-75186	19940809

PRIORITY APPLN. INFO.:	US 1993-109787	A	19930820
	US 1994-253531	A	19940603
	WO 1994-US8697	W	19940809

OTHER SOURCE(S): MARPAT 123:228913
GI



I

AB Title compds. [I; R1 = Me2CH, sec-Bu, Me3C, CMe2SMe, CMe2SOMe, CMe2SO2Me; R2 = (Z- or BOC-protected) N-methylalanyl, N-methyl-D-alanyl, Gly, N-methylglycyl, Pro, D-Pro, Ile], were prepared Thus, Me2NCH2CO2H and N-hydroxybenzotriazole in DMF were treated with EDC and then with (2R,3S)-3-(L-tert-butylglycinyl)amido-1-isoamyl-1-

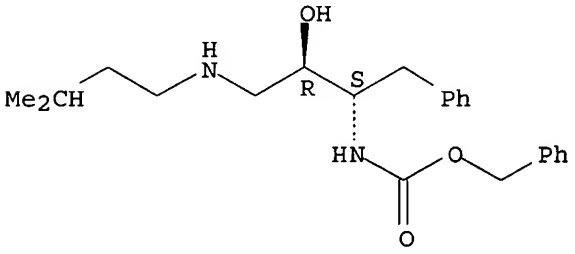
tert-butylcarbamoylamino-4-phenyl-2-butanol to give butanamide, 2-[(N,N-dimethylaminoacetyl)amino]-N-[3-[[[(1,1-dimethylethyl)amino]carbonyl]-(3-methylbutyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-3,3-dimethyl-, [1S-[1R*(R*),2S*]]. I inhibited HIV protease with IC50 = 6-2200 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:761481 CAPLUS

DOCUMENT NUMBER: 123:169509

TITLE: Cyclic sulfone containing retroviral protease inhibitors

INVENTOR(S): Bertenshaw, Deborah E.; Getman, Daniel; Heintz, Robert M.; Talley, John J.; Reed, Kathryn L.; Chruschiel, Robert Alan; Clare, Michael

PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.

SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9414793	A1	19940707	WO 1993-US11713	19931208
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5514801	A	19960507	US 1992-998187	19921229
CA 2153069	AA	19940707	CA 1993-2153069	19931208
AU 9457364	A1	19940719	AU 1994-57364	19931208
EP 677048	A1	19951018	EP 1994-903409	19931208
EP 677048	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08504815	T2	19960528	JP 1993-515176	19931208
AT 148113	E	19970215	AT 1994-903409	19931208
US 5849784	A	19981215	US 1995-556883	19951102

US 6265583	B1	20010724	US 1998-177100	19981022
US 6329524	B1	20011211	US 2001-870748	20010601
US 2002107264	A1	20020808	US 2001-973991	20011011
US 6552203	B2	20030422		
US 2004010143	A1	20040115	US 2003-369197	20030220
US 6875790	B2	20050405		
US 2005119257	A1	20050602	US 2004-932331	20040902

PRIORITY APPLN. INFO.: US 1992-998187 A 19921229

WO 1993-US11713 W 19931208

US 1995-556883 A3 19951102

US 1998-177100 A3 19981022

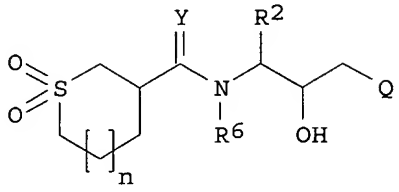
US 2001-870748 A1 20010601

US 2001-973991 A1 20011011

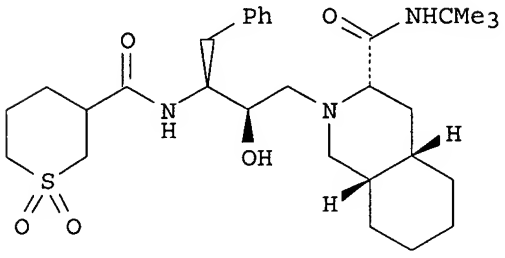
US 2003-369197 A1 20030220

OTHER SOURCE(S): MARPAT 123:169509

GI



I



II

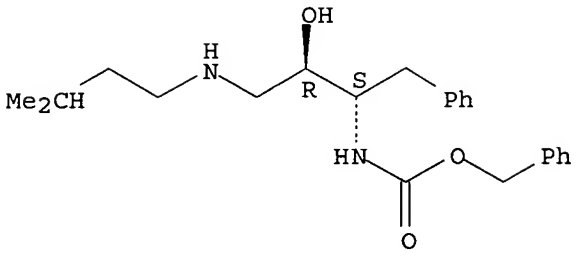
AB Cyclic sulfone moiety-containing hydroxyethylamine protease compds. and their use for pharmaceuticals, particularly as an inhibitor of HIV protease were disclosed. More narrowly claimed compds. were defined as I (Y = oxygen, sulfur, amino group; R2, R6 = substituent; substituted amino group; n = integer). A claimed example compound II was prepared II had activity as HIV protease inhibitor (IC50 = 3 nM).

IT **143225-04-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-(hydroxyalkyl)thiopyrancarboxamides and -thiomorpholinecarboxamides as virucides)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:408388 CAPLUS
DOCUMENT NUMBER: 122:188162
TITLE: preparation of sulfonylalkanoylamino hydroxyethylamino sulfamic acids as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; De Crescenzo, Gary A.; Sun, Eric T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9410136	A1	19940511	WO 1993-US10461	19931029
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2143191	AA	19940511	CA 1993-2143191	19931029
AU 9456651	A1	19940524	AU 1994-56651	19931029
EP 666843	A1	19950816	EP 1994-902199	19931029
EP 666843	B1	19990818		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 885881	A2	19981223	EP 1998-114522	19931029
EP 885881	A3	19991006		
EP 885881	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
EP 885880	A2	19981223	EP 1998-114523	19931029
EP 885880	A3	19991006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 183499	E	19990915	AT 1994-902199	19931029
ES 2134924	T3	19991016	ES 1994-902199	19931029
AT 234279	E	20030315	AT 1998-114522	19931029
PT 885881	T	20030731	PT 1998-114522	19931029
ES 2196436	T3	20031216	ES 1998-114522	19931029
EP 1462443	A1	20040929	EP 2004-7097	19931029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 5583132	A	19961210	US 1995-379645	19950202
GR 3031646	T3	20000229	GR 1999-402735	19991027

PRIORITY APPLN. INFO.: US 1992-969612 A 19921030
EP 1994-902199 A3 19931029
WO 1993-US10461 W 19931029
EP 1998-114523 A3 19980803

OTHER SOURCE(S): MARPAT 122:188162
GI

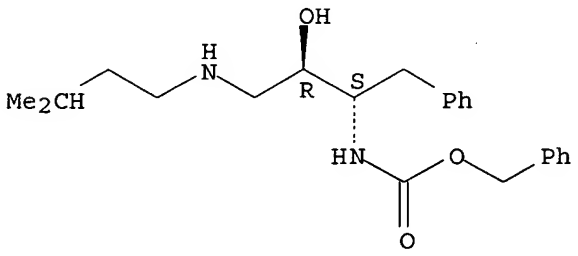
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Sulfonylalkanoylamino hydroxyamino sulfamic acid compds. [I; R = alkyl, alkenyl, alkynyl, cycloalkyl, hydroxyalkyl, etc.; R1, R20, R21 = H, CH2-SO2-NH2, CH2-CO2-Me, CO2Me, CONH2, etc.; R2 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, etc.; R3 = alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl; R4, R5 = H, any group in the definition of R3; R6 = H, alkyl; x = 1,2; t = 0, 1, 2; Y = O, S, NR15; R15 = H, any group in the definition of R3] and their pharmaceutically acceptable salts and esters, effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease, are prepared E.g., 2(S)-methyl-3-(methylsulfonyl)propionic acid was condensed with the phenylalanine derivative II (preparation given) in DMF containing HOBt and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide at 0° for 2 h and at room temperature for 16 h to give the title compound III. III was the only title compound prepared with data and it was not tested for biol. activities; however, some intermediates, e.g., analogs of II, were tested for their HIV inhibition activity.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation of sulfonylalkanoylamino hydroxyethylamino sulfamic acids as retroviral protease inhibitors)

RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:352211 CAPLUS
DOCUMENT NUMBER: 122:204547
TITLE: Inhibitors of HIV-1 Protease Containing the Novel

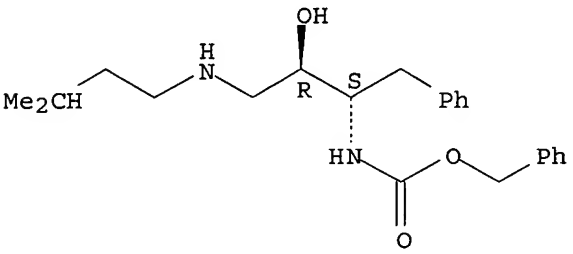
and Potent (R)-(Hydroxyethyl)sulfonamide Isostere
AUTHOR(S): Vazquez, Michael L.; Bryant, Martin L.; Clare, Michael; DeCrescenzo, Gary A.; Doherty, Elizabeth M.; Freskos, John N.; Getman, Daniel P.; Houseman, Kathryn A.; Julien, Janet A.; et al.
CORPORATE SOURCE: Searle Discovery Research, Skokie, IL, 60077, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(4), 581-4
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:204547

AB The authors have prepared and tested a series of novel and highly potent HIV-1 protease inhibitors based on the (R)-(hydroxyethyl)sulfonamide isostere. The isotere exhibits enhanced potency relative to the previously reported (hydroxyethyl)urea isotere. The preferred stereochem. for the critical hydroxyl group is R. X-ray crystallog. studies show that these inhibitors bind to the protease in an extended fashion with one of the sulfonamide oxygens forming a hydrogen bond to the key structural water mol. Some of the compds. showed excellent antiviral activity in vitro.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibitors of HIV-1 protease containing novel and potent (R)-(hydroxyethyl)sulfonamide isostere in relation to antiviral activity)

RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:340526 CAPLUS
DOCUMENT NUMBER: 122:133838
TITLE: preparation of succinoylamino hydroxyethylamino sulfamic acid derivatives as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; De Crescenzo, Gary A.; Sun, Eric T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9410133	A1	19940511	WO 1993-US10460	19931029
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2141570	AA	19940511	CA 1993-2141570	19931029
AU 9455892	A1	19940524	AU 1994-55892	19931029
EP 666841	A1	19950816	EP 1994-901230	19931029
EP 666841	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 148105	E	19970215	AT 1994-901230	19931029
ES 2097023	T3	19970316	ES 1994-901230	19931029
US 5602119	A	19970211	US 1995-379573	19950131
PRIORITY APPLN. INFO.:			US 1992-969683 A	19921030
			WO 1993-US10460 W	19931029

OTHER SOURCE(S): MARPAT 122:133838
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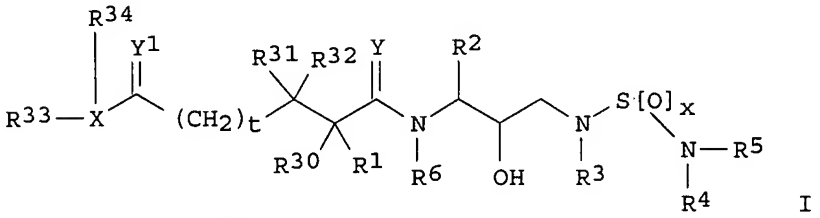

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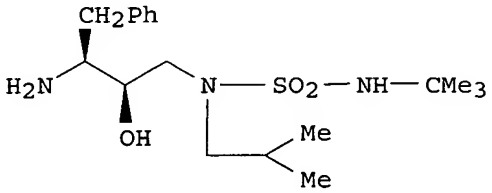

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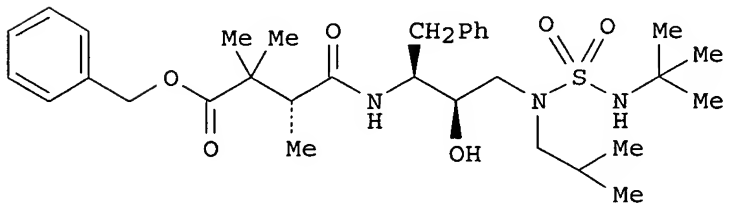


III

AB Title compds. [I; R1 = H, CH2-SO2-NH2, CH2-CO2Me, CO2Me, CONH2, CH2-CO-NHMe, CMe2-SH, etc.; R2 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, NO2, cyano, CF3, OH, SH, alkoxy, etc.; R3 = alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl,

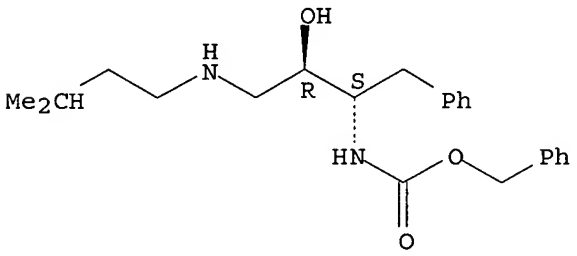
etc.; R4, R5 = H, any group in the definition of R3; R6 = H, alkyl; R30,R31,R32 = H, alkyl, alkenyl, alkynyl, etc.; R33, R34 = H, any group in the definition of R3, or R33 and R34 together with X = cycloalkyl, aryl, heterocyclyl, heteroaryl provided that when X = O, R34 = nil; X = N, O, CR17; R17 = H, alkyl; x = 1, 2; t = 0, 1, 2; Y, Y1 = O, S, NR15; R15 = H, any group in the definition of R3], effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease, are prepared Thus, 4-benzyl 2(R),3,3-trimethylsuccinate was condensed with the [(tert-butylaminosulfonyl)amino]propylamine derivative II (preparation given) in DMF containing HOBt and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride to give the title compound III. III had an IC50 of 1.4 μM against retroviral protease in an in vitro study. The title compds. were also compared with AZT in a CEM cell assay.

IT **143225-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1995:330514 CAPLUS
DOCUMENT NUMBER:	122:106521
TITLE:	Preparation of N-sulfamidohydroxyalkyl amino acid amides as retroviral protease inhibitors
INVENTOR(S):	Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Sun, Eric T.
PATENT ASSIGNEE(S):	G.D. Searle and Co., USA; Monsanto Co.
SOURCE:	PCT Int. Appl., 153 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9410134	A1	19940511	WO 1993-US10552	19931029

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2142997	AA	19940511	CA 1993-2142997	19931029
AU 9455470	A1	19940524	AU 1994-55470	19931029
EP 666842	A1	19950816	EP 1994-900506	19931029
EP 666842	B1	19980624		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 810208	A2	19971203	EP 1997-113206	19931029
EP 810208	A3	19981202		
EP 810208	B1	20020102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 167669	E	19980715	AT 1994-900506	19931029
ES 2118364	T3	19980916	ES 1994-900506	19931029
AT 211462	E	20020115	AT 1997-113206	19931029
PT 810208	T	20020628	PT 1997-113206	19931029
ES 2170305	T3	20020801	ES 1997-113206	19931029
US 6156768	A	20001205	US 1995-379545	19950202
US 6444678	B1	20020903	US 2000-633063	20000804
US 2003158236	A1	20030821	US 2002-178956	20020625
US 7037941	B2	20060502		
US 2005267214	A1	20051201	US 2005-167164	20050628
PRIORITY APPLN. INFO.:			US 1992-968730	A 19921030
			EP 1994-900506	A3 19931029
			WO 1993-US10552	W 19931029
			US 1995-379545	A3 19950202
			US 2000-633063	A1 20000804
			US 2002-178956	A3 20020625

OTHER SOURCE(S): MARPAT 122:106521

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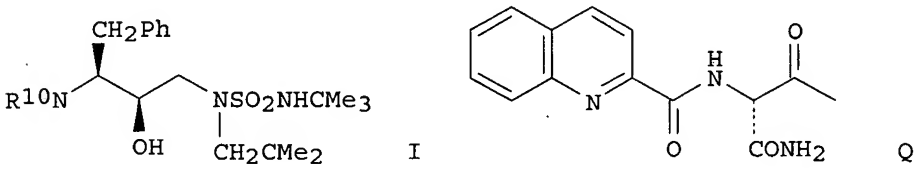
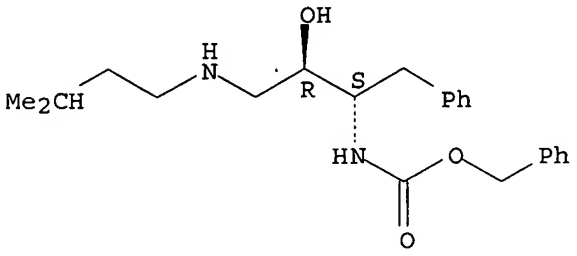


AB RR'N(CR7R8)tCHR1C(:Y)NR6CHR2CH(OH)CH2NR3SOxNR4R5 [R = H, (cyclo)alkyl, (hetero)aryl, alkyl(oxy)carbonyl, heterocyclyl(oxy)carbonyl, etc.; R' = groups cited for R3, R''SO2; R'' = groups cited for R3; NRR' = heterocyclyl, heteroaryl; R1,R7,R8 = H, (halo)alkyl, amino acid side chain, CONH2, CO2Me, etc.; R1R7 = atoms to form a cycloalkyl group; R2 = (un)substituted (cyclo)alkyl, aryl(alkyl); R3 = (cyclo)alkyl, (hetero)aryl(alkyl), aminoalkyl, etc.; R4,R5 = H, groups cited for R3; NR4R5 = heterocyclyl, heteroaryl; R6 = H, alkyl; Y = O, S, NH, NR3; t = 0-2; x = 1 or 2] were prepared Thus, N-benzyloxycarbonyl-3(S)-amino-1,2(S)-epoxy-4-phenylbutane (preparation given) was condensed with Me2CHCH2NH2 and the product amidated by ClSO2NHCMe3 (preparation given) to give, after deprotection, sulfamamide I (R10 = H) which was N-acylated by N-BOC-L-asparagine and the deprotected product N-acylated by quinoline-2-carboxylic acid to give I (R10 = quinolinoylasparaginyl group Q). The latter had IC50 of 2nM against HIV-1 infection of CEM cells in vitro.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of retroviral protease inhibitor)
RN 143225-04-1 CAPLUS
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:3862 CAPLUS
DOCUMENT NUMBER: 122:55727
TITLE: (Sulfonylalkanoylamino)(hydroxyethylamino)sulfonamides as HIV protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404493	A1	19940303	WO 1993-US7816	19930824
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 656888	A1	19950614	EP 1993-920214	19930824
EP 656888	B1	19980107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08500825	T2	19960130	JP 1993-506532	19930824
AU 669223	B2	19960530	AU 1993-50820	19930824
AU 9350820	A1	19940315		
AT 161828	E	19980115	AT 1993-920214	19930824
ES 2112430	T3	19980401	ES 1993-920214	19930824
RU 2146668	C1	20000320	RU 1995-106996	19930824
FI 9500651	A	19950214	FI 1995-651	19950214
NO 9500550	A	19950214	NO 1995-550	19950214
PRIORITY APPLN. INFO.:			US 1992-935071 A2	19920825

WO 1993-US7816 W 19930824

OTHER SOURCE(S): MARPAT 122:55727
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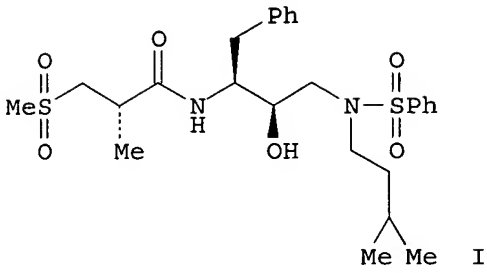


I

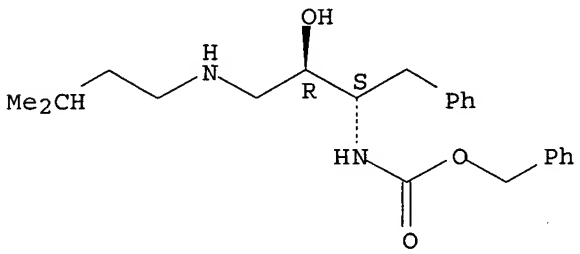
AB The title compds. RS(O)x(CH2)tC(R21)(R20)CH(R1)C(:Y)N(R6)CH(R2)C(OH)HC H2N(R3)S(O)xR4 [R = H, alkyl, alkenyl, alkynyl, heteroaryl, cycloalkyl, etc.; R1, R20, R21 = H, CH2SO2NH2, CH2CO2Me, CO2Me, CONH2, etc.; R2 = (un)substituted alkyl, aryl, cycloalkyl, arylkyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, alkynyl, etc.; R4 = alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, cycloalkyl, etc.; R6 = H, alkyl; Y = O, S, (un)substituted NH; t = 0, 1; x = 0-2], useful as HIV protease inhibitors for the treatment of AIDS, are prepared Thus, sulfonimide I was prepared and demonstrated IC50 against HIV protease of 3 nM.

IT **143225-04-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as HIV protease inhibitor)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

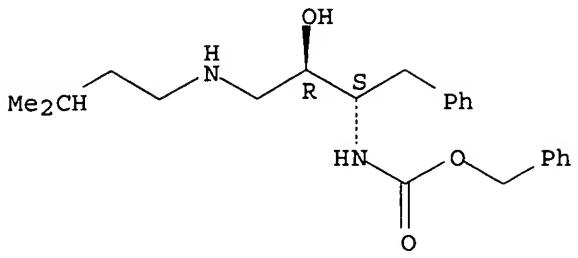


IT **143225-04-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of HIV protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

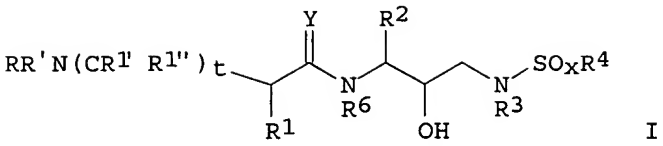


L3 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:701324 CAPLUS
DOCUMENT NUMBER: 121:301324
TITLE: Preparation of hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 198 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404492	A1	19940303	WO 1993-US7814	19930824
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9453474	A1	19940315	AU 1994-53474	19930824
AU 680635	B2	19970807		
EP 656887	A1	19950614	EP 1993-923714	19930824
EP 656887	B1	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08501288	T2	19960213	JP 1994-506530	19930824
JP 3657002	B2	20050608		
EP 810209	A2	19971203	EP 1997-113434	19930824
EP 810209	A3	19981202		
EP 810209	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 172717	E	19981115	AT 1993-923714	19930824
ES 2123065	T3	19990101	ES 1993-923714	19930824
RU 2173680	C2	20010920	RU 1995-106624	19930824
AT 218541	E	20020615	AT 1997-113434	19930824
PT 810209	T	20020930	PT 1997-113434	19930824
ES 2177868	T3	20021216	ES 1997-113434	19930824
US 6060476	A	20000509	US 1994-204827	19940302
US 5968942	A	19991019	US 1994-294468	19940823
NO 9500533	A	19950213	NO 1995-533	19950213
FI 9500650	A	19950214	FI 1995-650	19950214
FI 112471	B1	20031215		

US 6455581	B1	20020924	US 1995-451090	19950525
US 6046190	A	20000404	US 1996-586866	19960124
NO 9803099	A	19950213	NO 1998-3099	19980703
NO 307047	B1	20000131		
US 6248775	B1	20010619	US 1999-288080	19990408
US 6500832	B1	20021231	US 2000-525161	20000314
US 2002052399	A1	20020502	US 2001-798255	20010305
US 6417387	B2	20020709		
FI 2001002317	A	20011127	FI 2001-2317	20011127
US 2003191319	A1	20031009	US 2002-157019	20020530
US 6646010	B2	20031111		
US 2004044047	A1	20040304	US 2002-199481	20020722
US 6846954	B2	20050125		
US 6924286	B1	20050802	US 2003-633376	20030804
US 2004229922	A1	20041118	US 2004-812343	20040330
US 2005267171	A1	20051201	US 2005-110943	20050421
PRIORITY APPLN. INFO.:			US 1992-934984	A2 19920825
			EP 1993-923714	A3 19930824
			US 1993-110911	A2 19930824
			WO 1993-US7814	W 19930824
			US 1994-204827	A2 19940302
			US 1994-204872	B2 19940302
			US 1994-294468	A1 19940823
			WO 1994-US9139	W 19940823
			US 1995-451090	A3 19950525
			US 1999-288080	A1 19990408
			US 2001-798255	A1 20010305
			US 2002-157019	A1 20020530
			US 2002-199481	A3 20020722
			US 2003-633376	A1 20030804

OTHER SOURCE(S): MARPAT 121:301324
GI



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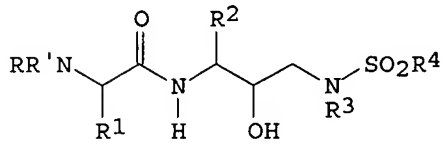

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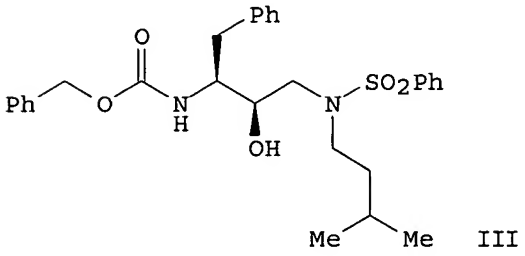


III

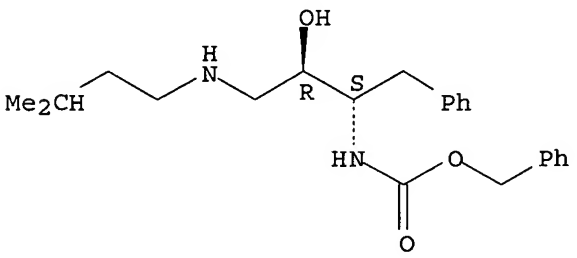
AB Title compds. [I and II; R = H, alkoxycarbonyl, aralkoxycarbonyl, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, heteroaryloxyalkyl, hydroxyalkyl, aryl, alkyl, alkenyl, alkynyl, substituted aminocarbonyl, etc.; R' = H, R3, R''SO2; RR'N = heterocyclyl, heteroaryl; R1 = H, CH2SO2NH2, CH2CO2Me, CO2Me, CONH2, CMe2SH, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, amino acid side chains, etc.; R1', R1'' = H, R1; 1 of R1', R1'' together with R1 form a cycloalkyl radical; R2 = (substituted) alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R3 = H, alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, aryl, aralkyl, heteroaralkyl, (substituted) aminoalkyl, etc.; R4 = R3, except H; R6 = H, alkyl; x = 0-2; t = 0, 1; Y = O, S, imino], were prepared Thus, title compound (III, solution phase preparation given) inhibited
HIV protease with IC50 = 16 nM.

IT **143225-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for HIV protease inhibitor)

RN 143225-04-1 CAPLUS

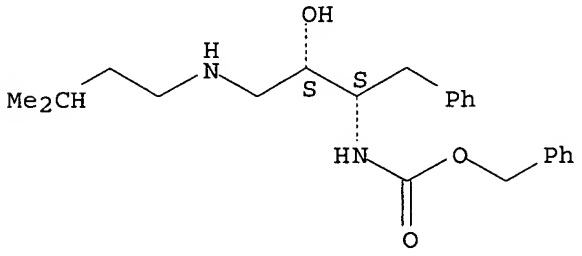
CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **159006-48-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of peptide derivative HIV protease inhibitor)
RN 159006-48-1 CAPLUS
CN Carbamic acid, [(1S,2S)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:680395 CAPLUS
DOCUMENT NUMBER: 121:280395
TITLE: Preparation of urea-containing hydroxyethylamine compounds as retroviral protease inhibitors
INVENTOR(S): Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Lin, Ko Chung; Vazquez, Michael L.; Mueller, Richard A.; Reed, Kathryn L.; Heintz, Robert M.; Clare, Michael; et al.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323368	A1	19931125	WO 1993-US4806	19930520
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342531	A1	19931213	AU 1993-42531	19930520
AT 141265	E	19960815	AT 1993-911369	19930520
ES 2091000	T3	19961016	ES 1993-911369	19930520
JP 2003160545	A2	20030603	JP 2002-337347	19930520
JP 2003192648	A2	20030709	JP 2002-337346	19930520
US 5648511	A	19970715	US 1995-452187	19950525
US 5510349	A	19960423	US 1995-471898	19950607
US 5610190	A	19970311	US 1995-476009	19950607
US 5872298	A	19990216	US 1997-833737	19970409
US 5872299	A	19990216	US 1997-854133	19970508
PRIORITY APPLN. INFO.:			US 1992-886558	A1 19920520

US 1990-615210	B2	19901119
US 1991-789646	B2	19911114
JP 1994-503847	A3	19930520
WO 1993-US4806	A	19930520
US 1993-152934	A3	19931115
US 1993-156498	B3	19931123
US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 121:280395

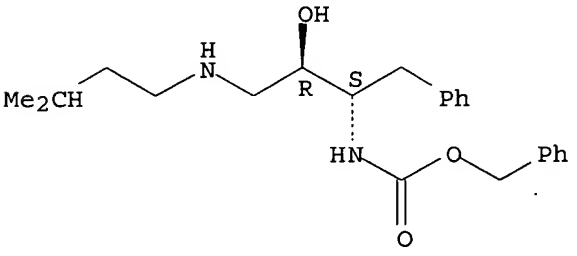
AB Title compds. ANR6CHR2CH(OH)CH2NR3C:YNR4R5 (A = R'SO2(CH2)tCR20R21CHR1C:Y'Me, etc., wherein R' = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, cycloalkyl, aryl heterocyclylalkyl, aralkyl, etc., t = 0,1; R1= H, H2NSO2CH2, MeO2C, MeNHCO, Me2NCO, MeNHCOCH2 H2NCO, etc.; R2 = alkyl,aryl, cycloalkyl, aralkyl, cycloalkylalkyl, etc.; R3 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, heteroaryl, heterocyclyl,etc.; R4, R5 = H, groups defined by R3, R4R5N = heterocyclylalkyl, heteroaryl; R6 = H, alkyl; Y = Y' = O, S; R20, R21 = groups defined by R1) effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease, are prepared. N-(benzyloxycarbonyl)-3(S)-amino-1,2(S)-epoxy-4-phenylbutane was reacted with 2-(aminomethyl)naphthalene to give (2R,3S)-N-[[3- (phenylmethylcarbamoyl)amino]-2-hydroxy-4-phenylbutyl]-N-[(-2-naphthylmethyl)]amine which in 3 steps was converted to the title compound [1S[1R(R),2S]]-N1[3-[[[(1,1-dimethylethyl)amino]carbonyl]-2-(naphthylmethyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(quinolylcarbonyl)amino]butanediamide (I). I inhibited HIV protease with IC50 of 2.9 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of HIV protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:579258 CAPLUS

DOCUMENT NUMBER: 121:179258

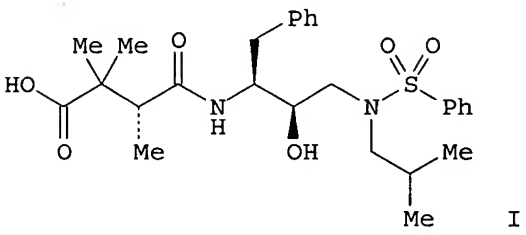
TITLE: N-(alkanoylamino-2-hydroxypropyl)sulfonamides useful as HIV protease inhibitors

INVENTOR(S): Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel; Decrescenzo, Gary A.; Freskos, John N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Monsanto Co.
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404491	A1	19940303	WO 1993-US7815	19930825
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 656886	A1	19950614	EP 1993-920213	19930824
EP 656886	B1	19970625		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08500824	T2	19960130	JP 1993-506531	19930824
AT 154800	E	19970715	AT 1993-920213	19930824
ES 2103488	T3	19970916	ES 1993-920213	19930824
AU 9350819	A1	19940315	AU 1993-50819	19930825
AU 674702	B2	19970109		
RU 2130016	C1	19990510	RU 1995-106823	19930825
NO 9500670	A	19950222	NO 1995-670	19950222
FI 9500841	A	19950223	FI 1995-841	19950223

PRIORITY APPLN. INFO.: US 1992-935490 A2 19920825
WO 1993-US7815 W 19930825

OTHER SOURCE(S): MARPAT 121:179258
GI



I

AB The title compds. R33(R34)X1C(:Y1)(CH2)tC(R31)(R32)C(R30)(R1)C(:Y)N(R6)C(R2)HC(OH)HCH2N(R3)S(O)xR4 [R1 = H, CH2SO2NH2, CO2Me, CONHMe, CONMe2, etc.; R2 = alkyl, aryl, cycloalkyl, (un)substituted cycloalkylalkyl and arylalkyl; R3 = H, alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, etc.; R4 = alkyl, haloalkyl alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl etc.; R6 = H, alkyl; R30-R32 = R1; R1R30R31 = cycloalkyl; R1R30R32C = cycloalkyl; R33, R34 = H, R3; R33R34X1 = cycloalkyl, aryl, heterocyclyl, etc.; X1 = O, N, CR17; R17 = H, alkyl; Y, Y1 = O, S,

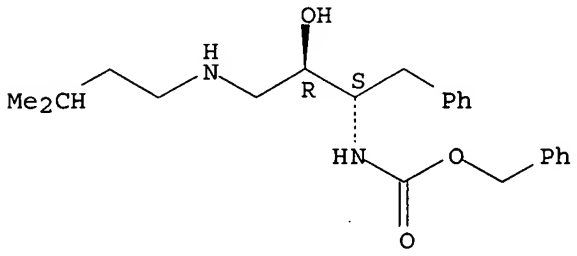
NR15; R15 = H, R3; t = 0, 1; x = 0-2], useful as HIV protease inhibitors for the treatment of AIDS, are prepared Thus, sulfonamide I was prepared and demonstrated IC50 against HIV protease of 1 nmol.

IT **143225-04-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as HIV protease inhibitor)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:603856 CAPLUS
DOCUMENT NUMBER: 119:203856
TITLE: Retroviral protease inhibitors
INVENTOR(S): Bertenshaw, Deborah Elizabeth; Freskos, John Nicholas; Getman, Daniel Paul; Heintz, Robert Martin; Lin, Ko Chung; Rogier, Donald Joseph, Jr.; Talley, John Jeffrey
PATENT ASSIGNEE(S): Monsanto Co., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208688	A1	19920529	WO 1991-US8617	19911118
W: AU, CA, CS, FI, HU, JP, KR, NO, PL, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2096409	AA	19920520	CA 1991-2096409	19911118
CA 2096409	C	20050208		
CA 2096525	AA	19920520	CA 1991-2096525	19911118
CA 2096525	C	20050208		
AU 9190531	A1	19920611	AU 1991-90531	19911118
EP 558603	A1	19930908	EP 1992-900449	19911118
EP 558603	B1	19980826		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06502860	T2	19940331	JP 1992-501088	19911118
EP 731088	A2	19960911	EP 1996-107359	19911118
EP 731088	A3	19970514		

EP 731088	B1	20001004			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 735019	A2	19961002	EP 1996-107357		19911118
EP 735019	A3	19970514			
EP 735019	B1	20000920			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 813867	A2	19971229	EP 1997-105350		19911118
EP 813867	A3	19980401			
EP 813867	B1	20050601			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 813868	A2	19971229	EP 1997-105352		19911118
EP 813868	A3	19980318			
EP 813868	B1	20050601			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 815856	A2	19980107	EP 1997-105351		19911118
EP 815856	A3	19980318			
EP 815856	B1	20050601			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AT 164839	E	19980415	AT 1992-901068		19911118
ES 2059295	T3	19980601	ES 1992-901068		19911118
AT 170169	E	19980915	AT 1992-900449		19911118
ES 2059293	T3	19981216	ES 1992-900449		19911118
AT 296624	E	20050615	AT 1997-105350		19911118
AT 296626	E	20050615	AT 1997-105351		19911118
AT 296625	E	20050615	AT 1997-105352		19911118
ES 2243958	T3	20051201	ES 1997-105350		19911118
ES 2243959	T3	20051201	ES 1997-105351		19911118
ES 2243960	T3	20051201	ES 1997-105352		19911118
ZA 9109163	A	19930519	ZA 1991-9163		19911119
ZA 9109164	A	19930519	ZA 1991-9164		19911119
ZA 9109160	A	19930819	ZA 1991-9160		19911119
ZA 9109161	A	19930819	ZA 1991-9161		19911119
ZA 9109162	A	19930819	ZA 1991-9162		19911119
US 5475027	A	19951212	US 1993-148817		19931108
US 5510378	A	19960423	US 1995-449974		19950525
US 5510487	A	19960423	US 1995-452603		19950525
US 5602175	A	19970211	US 1995-450606		19950525
US 5648511	A	19970715	US 1995-452187		19950525
US 5703076	A	19971230	US 1995-449966		19950525
US 5708004	A	19980113	US 1995-450605		19950525
US 5510349	A	19960423	US 1995-471898		19950607
US 5610190	A	19970311	US 1995-476009		19950607
US 5614522	A	19970325	US 1995-506213		19950724
US 5872298	A	19990216	US 1997-833737		19970409
US 5872299	A	19990216	US 1997-854133		19970508
GR 3034894	T3	20010228	GR 2000-402583		20001122
GR 3035176	T3	20010430	GR 2000-402865		20001229
PRIORITY APPLN. INFO.:			US 1990-615210	A2	19901119
			US 1991-789643	A	19911114
			US 1991-789644	B2	19911114
			US 1991-789645	B2	19911114
			US 1991-789646	B2	19911114
			EP 1992-901068	A3	19911118
			EP 1992-901691	A3	19911118

Searcher : Shears 571-272-2528

WO 1991-US8617	A	19911118
US 1992-886547	B1	19920520
US 1992-886556	B1	19920520
US 1992-886558	B2	19920520
US 1992-886663	B3	19920520
US 1993-148817	A3	19931108
US 1993-152934	A3	19931115
US 1993-156498	B3	19931123
US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 119:203856

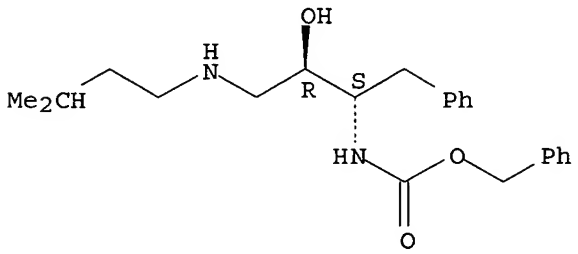
AB Urea-containing hydroxyethylamine protease inhibitor compds. RR1NCHR2CH(OH)CH2NR3C(Z)NR4R5 (R = H, acyl; R1, R4 = H, alkyl; R2 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R3 = alkyl, alkenyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaralkyl; R5 = alkyl; Z = O, S) were prepared, particularly as HIV inhibitors. Thus, 2,2-dimethyl-3-(4-pyridyl)propionic acid underwent Curtius rearrangement with diphenylphosphoryl azide and Et3N in toluene and the product was treated with 3(S)-[[N-(2-quinolinylcarbonyl)-L-asparaginyl]amino]-2(R)-hydroxy-4-phenyl-N-[(4-fluorophenyl)methyl]butylamine [2-C9H6NCO-Asn-NHCH(CH2Ph)CH(OH)CH2NRCH2C6H4F-p (I, 2-C9H6N = 2-quinolinyl, R = H] to afford I [R = [[1,1-dimethyl-2-(4-pyridyl)ethyl]amino]carbonyl]. This compound showed HIV protease inhibitory activity as follows: IC50 = 4 nM and ED50 = 37 nM.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of, with tert-Bu isocyanate)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:234479 CAPLUS
DOCUMENT NUMBER: 118:234479

TITLE: Preparation of sulfonylaminoamides as HIV protease inhibitors
INVENTOR(S): Reed, Kathryn Lea; Talley, John Jeffrey
PATENT ASSIGNEE(S): Monsanto Co., USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208699	A1	19920529	WO 1991-US8593	19911118
W: AU, CA, CS, FI, HU, JP, KR, NO, PL, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2096407	AA	19920520	CA 1991-2096407	19911118
AU 9191251	A1	19920611	AU 1991-91251	19911118
EP 558673	A1	19930908	EP 1992-902324	19911118
EP 558673	B1	19960417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06503092	T2	19940407	JP 1992-502639	19911118
AT 136888	E	19960515	AT 1992-902324	19911118
ES 2059296	T3	19960716	ES 1992-902324	19911118
EP 731088	A2	19960911	EP 1996-107359	19911118
EP 731088	A3	19970514		
EP 731088	B1	20001004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 735019	A2	19961002	EP 1996-107357	19911118
EP 735019	A3	19970514		
EP 735019	B1	20000920		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 813867	A2	19971229	EP 1997-105350	19911118
EP 813867	A3	19980401		
EP 813867	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 813868	A2	19971229	EP 1997-105352	19911118
EP 813868	A3	19980318		
EP 813868	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 815856	A2	19980107	EP 1997-105351	19911118
EP 815856	A3	19980318		
EP 815856	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5475027	A	19951212	US 1993-148817	19931108
US 5510378	A	19960423	US 1995-449974	19950525
US 5510487	A	19960423	US 1995-452603	19950525
US 5602175	A	19970211	US 1995-450606	19950525
US 5648511	A	19970715	US 1995-452187	19950525
US 5703076	A	19971230	US 1995-449966	19950525
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US 5610190	A	19970311	US 1995-476009	19950607
US 5614522	A	19970325	US 1995-506213	19950724
US 5872298	A	19990216	US 1997-833737	19970409
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GR 3034894	T3	20010228	GR 2000-402583	20001122
GR 3035176	T3	20010430	GR 2000-402865	20001229
PRIORITY APPLN. INFO.:			US 1990-615210 A	19901119

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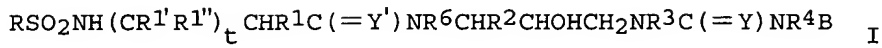
US 1991-789643	A	19911114
US 1991-789644	B2	19911114
US 1991-789646	B2	19911114
EP 1992-901068	A3	19911118
EP 1992-901691	A3	19911118
WO 1991-US8593	A	19911118
US 1992-886547	B1	19920520
US 1992-886556	B1	19920520
US 1992-886558	B2	19920520
US 1992-886663	B3	19920520
US 1993-148817	A3	19931108
US 1993-152934	A3	19931115
US 1993-156498	B3	19931123
US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 118:234479

GI



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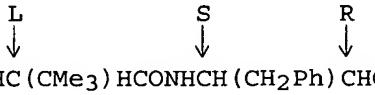


II

AB Title compds. I [R = (hydroxy)alkyl, alkenyl, cycloalkyl(alkyl), heterocycloalkyl, aryl, (hetero)aralkyl; t = 0, 1; R1 = CH2SO2NH2, (cyclo)alkyl, amino acid side chains selected from asparagine, glycine, leucine, phenylalanine, alanine, etc.; R1', R1'' = H, groups defined for R1; R2 = (cyclo)alkyl, aryl, etc.; R3 = (hydroxy)alkyl, alkenyl, cycloalkyl(alkyl), heterocycloalkyl, aryl, etc.; Y, Y' = O, S; B = R5, CR7R7'(CH2)nR8; R4, R5 = groups defined for R3; NR4R5 = heterocycloalkyl, heteroaryl; R6 = H, groups defined for R3; n = 0-6; R7, R7' = groups defined for R3, amino acid side chains selected from valine, isoleucine, glycine, alanine, asparagine, etc.; CR7R7' = cycloalkyl; R8 = cyano, OH, alkoxy, (cyclo)alkyl, etc.] were prepared as HIV protease inhibitors useful for the treatment of AIDS. Thus, N-(n-butylsulfonyl)-L-tert-butylglycine was coupled with (2R,3R)-3-amino-1-isoamyl-1-(tert-butylcarbamoyl)amino-4-phenyl-2-butanol in the presence of hydroxybenzotriazole and Me2N(CH2)3N:C:NEt.HCl in DMF to give title compound II. I had IC50 of

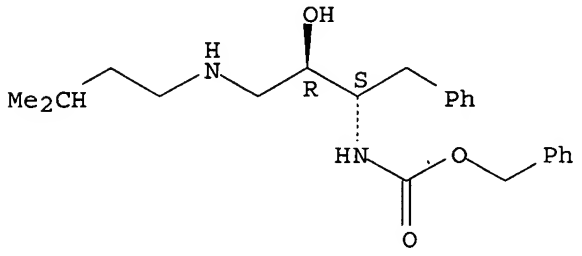
22-24 nM against HIV protease.

IT **143225-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for HIV protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:651772 CAPLUS

DOCUMENT NUMBER: 117:251772

TITLE: Preparation of N-(3-hydroxy-1-phenyl-4-ureido-2-butyl)asparaginamides and analogs as retroviral protease inhibitors

INVENTOR(S): Decrescenzo, Gary Anthony; Freskos, John Nicholas; Getman, Daniel Paul; Lin, Ko Chung; Rogier, Donald Joseph, Jr.; Talley, John Jeffrey

PATENT ASSIGNEE(S): Monsanto Co., USA

SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208698	A1	19920529	WO 1991-US8582	19911118
W: AU, CA, CS, FI, HU, JP, KR, NO, PL, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
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AU 662114	B2	19950824		
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EP 731088	A3	19970514		
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EP 813867	B1	20050601			
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US 5510487	A	19960423	US 1995-452603		19950525
US 5602175	A	19970211	US 1995-450606		19950525
US 5648511	A	19970715	US 1995-452187		19950525
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US 5610190	A	19970311	US 1995-476009		19950607
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			EP 1992-901068	A3	19911118
			EP 1992-901691	A3	19911118
			WO 1991-US8582	A	19911118
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			US 1993-148817	A3	19931108
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OTHER SOURCE(S): MARPAT 117:251772
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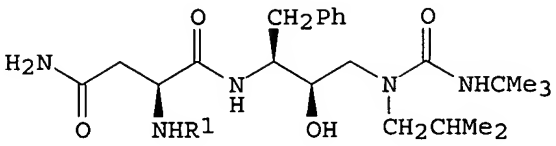


I

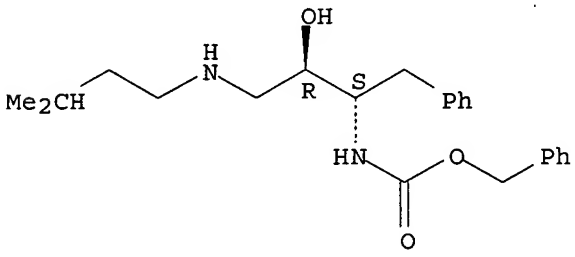
AB ANR6CHR2CH(OH)CH2NR3C(:Y)NR4B [A = R, R11X1C(:Y1), etc.; B = R5, CHR7COR8; R = H, (ar)alkoxycarbonyl, alkanoyl, aroyl, alkyl, aryl, etc.; R2 = (cyclo)alkyl, aryl, aralkyl, etc.; R3 - R6, R11 = H, (cyclo)alkyl, alkenyl, aryl, aralkyl, etc.; R7 = H, amino acid side chain; R8 = amino acid residue; X1 = O, N, CH2, alkylidene, etc.; Y, Y1 = O, S] were prepared Thus, L-PhCH2O2CNHCH(CH2Ph)COCH2Cl was reduced and the product converted to the epoxide which was condensed with Me2CHCH2NH2 to give, after condensation with Me3CNCO and deprotection, 1-ureido-2-butanol (2R,3S)-H2NCH(CH2Ph)CH(OH)CH2N(CH2CHMe2)CONHCMe3 which was condensed with Z-Asn-OH to give title compound I (R1 = CO2CH2Ph). The latter was deprotected and the product condensed with 2-quinolinecarboxylic acid N-hydroxysuccinimide ester to give I (R1 = 2-quinolinecarbonyl) which had IC50 of 7 nM against HIV protease in vitro.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:651771 CAPLUS
DOCUMENT NUMBER: 117:251771
TITLE: Preparation of N-(3-hydroxy-1-phenyl-4-ureido-2-butyl)asparaginamides and analogs as retroviral protease inhibitors
INVENTOR(S): Clare, Michael; Decrescenzo, Gary Anthony; Freskos, John Nicholas; Getman, Daniel Paul; Heintz, Robert Martin; Lin, Ko Chung; Mueller, Richard August; Reed, Kathryn Lea; Talley, John Jeffrey; et al.

PATENT ASSIGNEE(S): Monsanto Co., USA; G.D. Searle and Co.
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208701	A1	19920529	WO 1991-US8613	19911118
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RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
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AU 9190925	A1	19920611	AU 1991-90925	19911118
AU 661667	B2	19950803		
EP 558630	A1	19930908	EP 1992-901068	19911118
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JP 06505963	T2	19940707	JP 1992-501319	19911118
EP 731088	A2	19960911	EP 1996-107359	19911118
EP 731088	A3	19970514		
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 735019	A2	19961002	EP 1996-107357	19911118
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EP 813868	A2	19971229	EP 1997-105352	19911118
EP 813868	A3	19980318		
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ES 2059293	T3	19981216	ES 1992-900449	19911118
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ES 2243959	T3	20051201	ES 1997-105351	19911118
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			EP 1992-901068	A3 19911118
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			WO 1991-US8613	A 19911118
			US 1992-886547	B1 19920520
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OTHER SOURCE(S): MARPAT 117:251771
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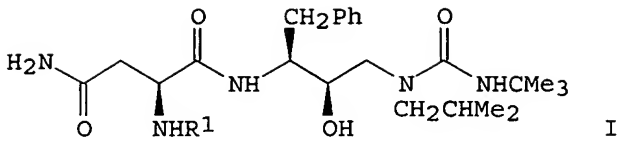


I

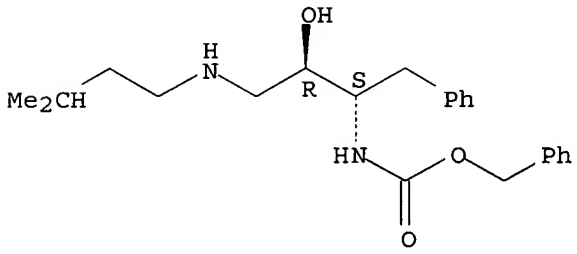
AB ANR6CHR2CH(OH)CH2NR3C(:Y)NR4R5 [A = R7SO2(CH2)tCR20R21CHR1C(:Y1), RR7N(CR10R11)tCHR1CO, R33R34X1C(:Y2)(CH2)tCR31R32CR1R30C(:Y1); R = H, (ar)alkanoyl), (hetero)aroyl, (ar)alkoxycarbonyl, etc.; R1, R10, R11 = H, CH2SO2NH2, CO2Me, CONH2, (cyclo)alkyl, amino acid side chain; R2 = (cyclo)alkyl, aryl, aralkyl, etc.; R3 = (cyclo)alkyl, alkenyl, aryl, aralkyl, etc.; R4, R5, R7, R33, R34 = H, groups cited for R3; or NR4R5, NRR7 = heterocyclyl, heteroaryl; R20, R21, R30, R31, R32 = groups cited for R1; 1 of R1 or R30 with 1 of R31 or R32 = atoms to form a carbocyclic ring; X1 = O, N, CR17; R17 = H, alkyl (when X1 = O, R34 = null); or X1R33R34 = cycloalkyl, (hetero)aryl, heterocyclyl; Y, Y1, Y2 = O, S; t = 0, 1] were prepared Thus, L-PhCH2O2CNHCH(CH2Ph)COCH2Cl was reduced and the product converted to the epoxide which was condensed with Me2CHCH2NH2 to give, after condensation with Me3CNCO and deprotection, 1-ureido-2-butanol (2R,3S)-H2NCH(CH2Ph)CH(OH)CH2N(CH2CHMe2)CONHCMe3 which was condensed with Z-Asn-OH to give title compound I (R1 = CO2CH2Ph). The latter was deprotected and the product condensed with 2-quinolinecarboxylic and N-hydroxysuccinimide ester to give I (R1 = 2-quinolinecarbonyl) which had IC50 of 7 nM against HIV protease in vitro.

IT **143225-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of retroviral protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:531559 CAPLUS

DOCUMENT NUMBER: 117:131559

TITLE: Preparation of amino acid amides as HIV protease inhibitors

INVENTOR(S): Reed, Kathryn Lea; Talley, John Jeffrey

PATENT ASSIGNEE(S): Monsanto Co., USA

SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208700	A1	19920529	WO 1991-US8596	19911118
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AU 662309	B2	19950831		
EP 558657	A1	19930908	EP 1992-901691	19911118
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US 1993-156498	B3	19931123
US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 117:131559

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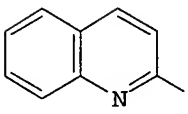


CO-Asn-NHCH(CH_2Ph)CHOHCH$_2$NH(CH_2CHMe$_2$)CONHCMe$_3$ II

AB Title compds. R6ANCHR2CHOHCH2NR3C(:Y)XR4R5 [I; A = R1SO2(CH2)tCR20R21CHR1C(:Y'), RR'N(CR1'R1'')tCHR1CO, R33R34X'C(:Y'')(CH2)tCR31R32CR1R30C(:Y'); R = H, alkoxycarbonyl, aralkoxycarbonyl, alkanoyl, cycloalkylcarbonyl, heterocyclylcarbonyl, etc.; R' = H, groups defined for R3 or NRR' = heterocycloalkyl, heteroaryl; t = 0, 1; R1 = CH2SO2NH2, H, alkyl, cycloalkyl, amino acid side chains selected from asparagine, glycine, leucine, alanine, etc.; R1', R1'' = H, groups defined for R1; R2 = (substituted) alkyl, -aryl, -cycloalkyl, -cycloalkylalkyl, -aralkyl; R3 = alkyl, alkenyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, aryl, etc.; X = O, CR17; R17 H, alkyl; X' = N, O, CR17; R5 and/or R34 is absent when X and/or X' = O; Y, Y', Y'' = O, S; R4, R5 = H, groups defined for R3 or CR4R5 = cycloalkyl, aryl, heteroaryl, heterocycloalkyl; R6 = H, groups defined for R3; R20, R21, R30, R31, R32 = groups defined for R1 or one of R1 and R30 together with one of R31 and R32 and the C atoms to which they are attached form a cycloalkyl group; or R30R32 = atoms to complete a C3-6 cycloalkyl; R33, R34 = H, groups defined for R3; or X'R33R34 = cycloalkyl, aryl, heterocyclyl, heteroaryl] were prepared Thus, 2-(R),

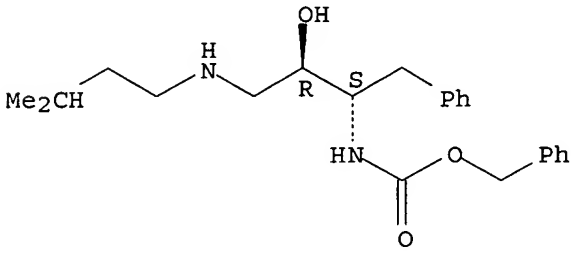
3-(S)-N-[[3-amino]-2-hydroxy-4-phenyl]-1-[(2-methylpropyl)amino-1-(1,1-dimethylethyl)amino]carbonyl]butane (preparation given) was coupled with Z-Asn-OH and the product was successively hydrogenated then coupled with 2-quinolinecarboxylic acid N-hydroxysuccinimide ester to give [1S-[1R*(R*),2S*]]-II. I had IC50's of 21 nM - 1.6 mM for inhibition of HIV protease.

IT **143225-04-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for HIV protease inhibitors)

RN 143225-04-1 CAPLUS

CN Carbamic acid, [(1S,2R)-2-hydroxy-3-[(3-methylbutyl)amino]-1-(phenylmethyl)propyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



FILE 'CAOLD' ENTERED AT 16:25:20 ON 15 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L4 0 L2

FILE 'USPATFULL' ENTERED AT 16:28:01 ON 15 JUN 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Jun 2006 (20060615/PD)
FILE LAST UPDATED: 15 Jun 2006 (20060615/ED)
HIGHEST GRANTED PATENT NUMBER: US7062785
HIGHEST APPLICATION PUBLICATION NUMBER: US2006130207
CA INDEXING IS CURRENT THROUGH 15 Jun 2006 (20060615/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jun 2006 (20060615/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

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FILE 'MEDLINE' ENTERED AT 16:28:57 ON 15 JUN 2006

FILE 'BIOSIS' ENTERED AT 16:28:57 ON 15 JUN 2006
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L7            0 L2

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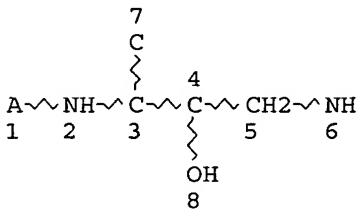

Str. II

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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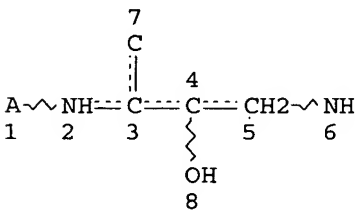


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STEREO ATTRIBUTES: NONE
L11 8394 SEA FILE=REGISTRY SUB=L9 SSS FUL L10

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SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 16:31:41 ON 15 JUN 2006
L12 381 S L11

L14 44 SEA ABB=ON PLU=ON L12(L)((RETROVIR? OR RETRO(W)(VIRUS OR VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A)INHIBIT?
L15 12 SEA ABB=ON PLU=ON L14 NOT L3

E1 THROUGH E421 ASSIGNED

L15 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 15 May 2006
ACCESSION NUMBER: 2006:449362 CAPLUS
TITLE: Process for the preparation of pyrimidinyl aminodiphenylhexane derivatives as retroviral protease inhibiting prodrugs
INVENTOR(S): Kumar, Gondi N.; Herrin, Thomas R.; Kempf, Dale J.; Betebenner, David A.; Chen, Xiaoqi; Norbeck, Daniel W.; Sham, Hing Leung; Patel, Ketan M.; Liu, Jih-Hua; Tien, Jieh-Heh J.; Stoner, Eric J.; Stengel, Peter J.; Plata, Daniel J.; Oliver, Patricia A.; Kolaczkowski, Lawrence; Hannick, Steven M.; Dickman, Daniel A.; Cooper, Arthur J.; Condon, Stephen L.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Aust. Pat. Appl., 252 pp.
CODEN: AUXXCM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2004201149	A1	20040422	AU 2004-201149	20040318
PRIORITY APPLN. INFO.:			AU 2001-13690 A3	20010112

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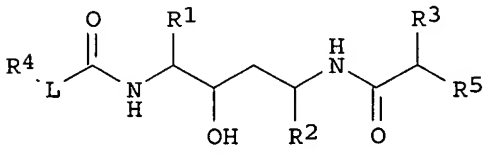

I

AB Pyrimidinyl aminodiphenylhexane derivs. I, wherein R1 and R2 are independently lower alkyl, cycloalkyl-alkyl, aryl-alkyl; R3 is lower alkyl, cycloalkyl-alkyl, hydroxy-alkyl; R4 is aryl, heterocyclic; R5 is five- or six-membered heterocycle containing at least one nitrogen atom; L is O, S, NH, N-alkyl, , N-cycloalkyl, N-cycloalkyl-alkyl, O-alkylenyl, SO-alkylenyl, S(O)2-alkylenyl, alkylenyl-O, alkylenyl-S,

alkylenyl, alkenylenyl, were prepared and tested in vitro and in human as retroviral protease inhibiting prodrugs. Thus, (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(1-tetrahydropyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane was prepared via coupling of (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane with 2S-(1-tetrahydro-pyrimid-2-onyl)-3-methylbutanoic acid. The present invention relates to novel compds. and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for inhibiting a retroviral infection and in particular an HIV infection, processes for making the compds. and synthetic intermediates employed in the processes. While the compound of the invention can be administered as the sole active pharmaceutical agent, it can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents, or vaccines. The compds. of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). Total daily dose administered to a human or other mammal host in single or divided doses may be in amts., for example, from 0.001 to 300 mg/kg body weight daily and more usually 0.1 to 20 mg/kg body weight daily.

IT INDEXING IN PROGRESS

IT **161302-40-5P**

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as **retroviral protease inhibiting** prodrugs)

L15 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 22 Sep 2005

ACCESSION NUMBER: 2005:1021739 CAPLUS

DOCUMENT NUMBER: 143:326208

TITLE: Preparation of diamino-mono-ol dipeptide isostere core based resistance-repellent retroviral protease inhibitors

INVENTOR(S): Eissenstat, Michael; Guerassina, Tatiana

PATENT ASSIGNEE(S): Sequoia Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087728	A1	20050922	WO 2005-US8381	20050311

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC,

NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005209301 A1 20050922 US 2005-77135 20050311

PRIORITY APPLN. INFO.: US 2004-552643P P 20040311

OTHER SOURCE(S): MARPAT 143:326208

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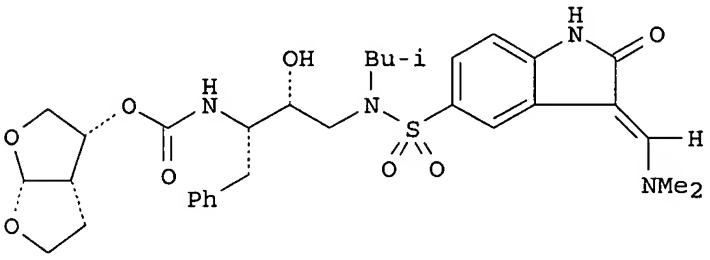


II

AB Title compds. X-A-B-A'-X' [X = 5-7 membered non-aromatic heterocycle; A = ZCZNH, ZCOCONH, ZSO2NH, etc.; Z = amino, O, S, etc.; B = syn-CH(D)CH(OH)CH2; D = alk(en/yn)yl; aryl, cycloalkyl, etc.; A' = ND'-E'; D' = alk(en/yn)yl, aryl, cycloalkyl, etc.; E' = CO, SO, SO2; X' = indolyl; I] are prepared For instance, II is prepared in several steps from 2-oxo-2,3-dihydro-1H-indol-5-sulfonyl chloride (preparation given), [1-benzyl-2-hydroxy-4-phenylbutyl]isobutylcarbamic acid benzyl ester, carbonic acid 2,5-dioxopyrrolidin-1-yl ester hexahydrofuro[2,3-b]furan-3-yl ester and DMF di-Me acetal. II has an IC50 = 93 nM for a recombinant wild type HIV protease. I are useful for treating HIV infections.

IT **160232-08-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diamino-mono-ol dipeptide isostere core based resistance-repellent **retroviral protease inhibitors**)

IT **664344-42-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diamino-mono-ol dipeptide isostere core based resistance-repellent **retroviral protease inhibitors**)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 11 Jan 2001

ACCESSION NUMBER: 2001:25780 CAPLUS

DOCUMENT NUMBER: 134:86548

TITLE: Preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors

INVENTOR(S): Getman, Daniel P.; De Crescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Deyadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 85 pp., Cont.-in-part of U. S. Ser. No.

402,419, abandoned
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

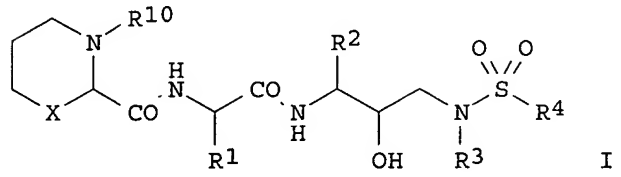
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6172101	B1	20010109	US 1998-894984	19980423
WO 9628465	A1	19960919	WO 1996-US2683	19960307

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

PRIORITY APPLN. INFO.: US 1995-402419 B2 19950310
WO 1996-US2683 W 19960307
US 1995-474117 A2 19950607

OTHER SOURCE(S): MARPAT 134:86548
GI



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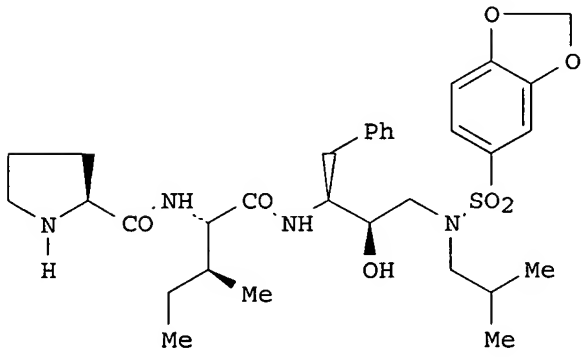

II

AB Heterocyclylcarbonyl amino acids, such as I [R1 = alkyl, alkenyl, alkynyl, etc.; R2 = alkyl, arylalkyl, alkylthioalkyl, arylthioalkyl, etc.; R3 = alkyl, cycloalkyl; R4 = aryl, heteroaryl; R10 = H, alkyl, nitrogen protecting group, etc., X = CH2, bond], were prepared for pharmaceutical use as HIV protease inhibitors for inhibiting retroviral proteases, such as human immunodeficiency virus (HIV) protease, prophylactically preventing retroviral infection or the spread of a retrovirus, and treatment of a retroviral infection. Thus, II was prepared by a multistep synthetic sequence starting from N-protected-L-phenylalanine, -L-isoleucine, -L-proline, isobutylamine,

and 1,3-benzodioxole. The prepared heterocyclylcarbonyl amino acids were tested via an HIV inhibition assay.

IT **143224-62-8P 160232-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide **retroviral protease inhibitors**)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Nov 2000
ACCESSION NUMBER: 2000:821607 CAPLUS
DOCUMENT NUMBER: 133:350519
TITLE: Synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan Raj; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 148 pp., Cont.-in-part of U.S. Ser. No. 402,450, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6150556	A	20001121	US 1995-479071	19950607
CA 2215025	AA	19960919	CA 1996-2215025	19960307
WO 9628464	A1	19960919	WO 1996-US2685	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
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AU 9653561	A1	19961002	AU 1996-53561	19960307
AU 704360	B2	19990422		
BR 9607543	A	19971223	BR 1996-7543	19960307
EP 813543	A1	19971229	EP 1996-910337	19960307
EP 813543	B1	20050914		
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CN 1196732	A	19981021	CN 1996-193618	19960307
JP 11501921	T2	19990216	JP 1996-527649	19960307
EP 1076062	A1	20010214	EP 2000-114911	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
EP 1188766	A1	20020320	EP 2001-129219	19960307
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PL 185108	B1	20030228	PL 1996-322163	19960307

PL 185543	B1	20030530	PL 1996-352508	19960307
EE 4376	B1	20041015	EE 1997-200	19960307
CZ 294966	B6	20050413	CZ 1997-2825	19960307
AT 304550	E	20050915	AT 1996-910337	19960307
ES 2249779	T3	20060401	ES 1996-910337	19960307
NO 9704149	A	19971105	NO 1997-4149	19970909
US 6316496	B1	20011113	US 2000-495334	20000201
US 6388132	B1	20020514	US 2000-694783	20001024
US 2003204097	A1	20031030	US 2002-97642	20020315
US 6683210	B2	20040127		
US 6861539	B1	20050301	US 2003-638479	20030812
US 2005227926	A1	20051013	US 2005-36606	20050118
PRIORITY APPLN. INFO.:			US 1995-402450	B2 19950310
			US 1995-479071	A 19950607
			EP 1996-910337	A3 19960307
			WO 1996-US2685	W 19960307
			US 1998-913096	A1 19980121
			US 2000-495334	A1 20000201
			US 2000-694783	A1 20001024
			US 2002-97642	A1 20020315
			US 2003-638479	A1 20030812

OTHER SOURCE(S): MARPAT 133:350519

AB Peptides R13NHCH2CONHCHR1CONHCH(CH2Ph)CH(OH)CH2N(Bu-i)SO2R4 (R1 = C1-5alkyl, C2-5alkynyl; R4 = aryl; R13 = aralkyl, cycloalkyl, alkoxyalkyl), including stereoisomers, pharmaceutically acceptable salts, and prodrugs, were prepared as retroviral protease inhibitors. Thus, compound 2S-[[(methylamino)acetyl]amino]-N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-3,3-dimethylbutanamide was prepared and shown to be an effective HIV protease inhibitor (IC50 = 2 nM, EC50 = 18 nM).

IT **143224-62-8P 160232-08-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide **retroviral protease inhibitors**)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 09 Nov 2000
ACCESSION NUMBER: 2000:784383 CAPLUS
DOCUMENT NUMBER: 133:335463
TITLE: Synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Belekudru; Nagarajan, Srinivasan Raj; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 148 pp., Cont.-in-part of U.S. Ser. No.

402,450, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6143788	A	20001107	US 1998-913096	19980121
WO 9628464	A1	19960919	WO 1996-US2685	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
EP 1188766	A1	20020320	EP 2001-129219	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
US 6388132	B1	20020514	US 2000-694783	20001024
US 2003204097	A1	20031030	US 2002-97642	20020315
US 6683210	B2	20040127		
US 6861539	B1	20050301	US 2003-638479	20030812
US 2005227926	A1	20051013	US 2005-36606	20050118

PRIORITY APPLN. INFO.:	US 1995-402450	B2	19950310
	WO 1996-US2685	W	19960307
	US 1995-479071	A	19950607
	EP 1996-910337	A3	19960307
	US 1998-913096	A1	19980121
	US 2000-495334	A1	20000201
	US 2000-694783	A1	20001024
	US 2002-97642	A1	20020315
	US 2003-638479	A1	20030812

OTHER SOURCE(S): MARPAT 133:335463
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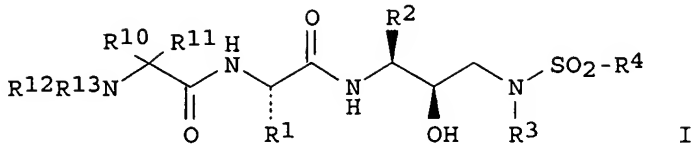

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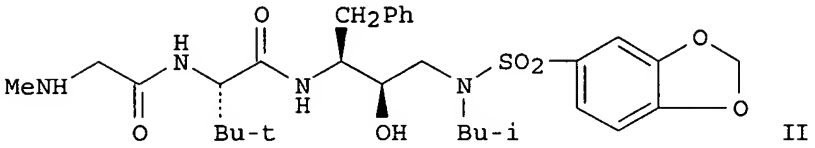

II

AB Peptides I [R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2S(O)Me, CH2SO2Me, CMe2SMe, CMe2S(O)Me, CMe2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl or benzo-fused 5-6 membered heteroaryl or heterocyclyl; R10 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R11 = any group given for R10 or benzyl, imidazolylmethyl, CH2CH2CONH2, CH2CONH2, CH2CH2SMe, CH2SMe or sulfone or sulfoxide derivs.; R12, R13 = H, alkyl, aralkyl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, aryl or heteroaryl, where cycloalkyl or heteroaryl may be benzo fused (with provisos)] were prepared as retroviral protease inhibitors. Thus, compound II was prepared and shown to be an effective HIV protease inhibitor (IC50 = 2 nM, EC50 = 18 nM).

IT **143224-62-8P 160232-08-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide **retroviral protease inhibitors**)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 05 Apr 1999
ACCESSION NUMBER: 1999:212791 CAPLUS
DOCUMENT NUMBER: 130:262109
TITLE: Polar substituted hydrocarbon retroviral protease inhibitors and prodrugs, and preparation thereof
INVENTOR(S): Grobelny, Damian Wojciech
PATENT ASSIGNEE(S): Narhex Ltd., Hong Kong
SOURCE: U.S., 102 pp., Cont.-in-part of U.S. 5,679,688.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5888992	A	19990330	US 1996-612894	19960429
ZA 9406952	A	19950413	ZA 1994-6952	19940909
WO 9507269	A1	19950316	WO 1994-AU538	19940912
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5679688	A	19971021	US 1994-295855	19941104
US 6071895	A	20000606	US 1999-255551	19990222
PRIORITY APPLN. INFO.:			AU 1992-1304 A	19920311
			AU 1993-1161 A	19930910
			AU 1994-6446 A	19940624
			WO 1994-AU538 W	19940912
			US 1994-295855 A2	19941104
			WO 1993-AU103 W	19930311

OTHER SOURCE(S): MARPAT 130:262109

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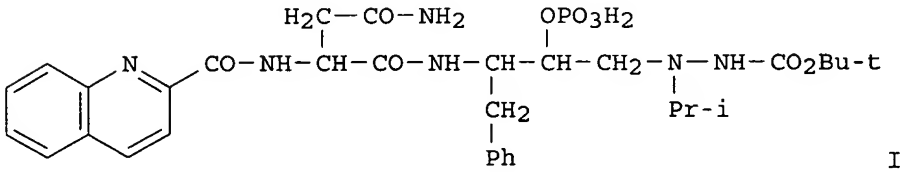

I

AB The title retroviral protease inhibitors, and related prodrugs having a solubilizing group which is labile in vivo, are provided. Preparation of e.g. the disodium salt of I is described. Transformation of prodrug to drug was shown in pharmacokinetic expts.

IT **221898-05-1D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polar substituted hydrocarbon **retroviral protease inhibitors** and prodrugs, and preparation thereof)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 21 Dec 1996
ACCESSION NUMBER: 1996:748344 CAPLUS
DOCUMENT NUMBER: 126:19331
TITLE: Preparation of peptide hydroxyethylaminosulfonamide analogs as retroviral

protease inhibitors.

INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; Mcdonald, Joseph J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628463	A1	19960919	WO 1996-US2684	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5756533	A	19980526	US 1995-474052	19950607
AU 9650294	A1	19961002	AU 1996-50294	19960307
AU 705268	B2	19990520		
EP 813542	A1	19971229	EP 1996-907135	19960307
EP 813542	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
BR 9607638	A	19980526	BR 1996-7638	19960307
JP 2001513746	T2	20010904	JP 1996-527648	19960307
AT 226213	E	20021115	AT 1996-907135	19960307
EP 1258491	A1	20021120	EP 2002-11526	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
PL 184748	B1	20021231	PL 1996-322784	19960307
EE 4349	B1	20040816	EE 1997-201	19960307
NO 9704148	A	19971027	NO 1997-4148	19970909
US 5968970	A	19991019	US 1998-894900	19980102
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		

PRIORITY APPLN. INFO.:	US 1995-402287	A2	19950310
	US 1995-474052	A2	19950607
	EP 1996-907135	A3	19960307
	WO 1996-US2684	W	19960307
	US 1999-451920	A3	19991201

OTHER SOURCE(S): MARPAT 126:19331

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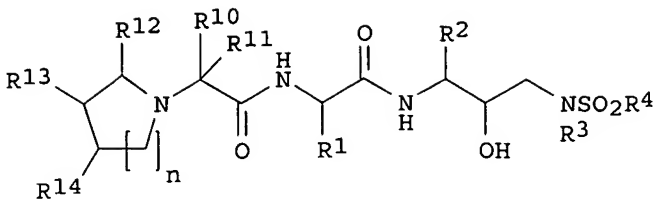

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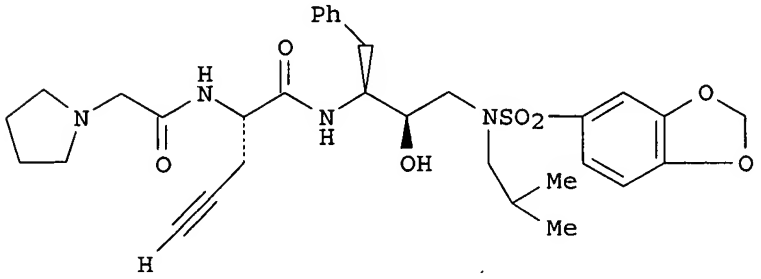

II

AB Title compds. (I; n = 1, 2; R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl,, cyanoalkyl, imidazolylalkyl, CH2CONH2, CH2SOMe, etc.; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzoheteroaryl; R10 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl, PhCH2, imidazolylmethyl, CH2CH2CONH2, CH2CH2SMe, etc.; R12 = H, hydroxyalkyl, alkoxyalkyl; R13, R14 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, alkoxyalkyl; R12R13, R13R14 = atoms to form 5-6 membered heteroaryl or benzo rings), were prepared Thus, title compound (II), prepared by solution phase means, inhibited HIV protease with IC50 = 2 nM.

IT **183553-44-8P 183553-45-9P 183554-06-5P 183812-52-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylaminosulfonamide **retroviral protease inhibitors**)

L15 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 14 Dec 1996
ACCESSION NUMBER: 1996:733943 CAPLUS
DOCUMENT NUMBER: 126:8710
TITLE: Preparation of bisamino acid hydroxyethylaminosulfonamide retroviral protease inhibitors.
INVENTOR(S): Getman, Daniel P.; Descrescenzo, Gary A.; Freskos, John N.; Vasquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; Mcdonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9628464	A1	19960919	WO 1996-US2685	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 6150556	A	20001121	US 1995-479071	19950607
AU 9653561	A1	19961002	AU 1996-53561	19960307
AU 704360	B2	19990422		
BR 9607543	A	19971223	BR 1996-7543	19960307
EP 813543	A1	19971229	EP 1996-910337	19960307
EP 813543	B1	20050914		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
JP 11501921	T2	19990216	JP 1996-527649	19960307
EP 1188766	A1	20020320	EP 2001-129219	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
PL 185108	B1	20030228	PL 1996-322163	19960307
PL 185543	B1	20030530	PL 1996-352508	19960307
EE 4376	B1	20041015	EE 1997-200	19960307
AT 304550	E	20050915	AT 1996-910337	19960307
NO 9704149	A	19971105	NO 1997-4149	19970909
US 6143788	A	20001107	US 1998-913096	19980121
PRIORITY APPLN. INFO.:			US 1995-402450	A2 19950310
			US 1995-479071	A 19950607
			EP 1996-910337	A3 19960307
			WO 1996-US2685	W 19960307

OTHER SOURCE(S): MARPAT 126:8710

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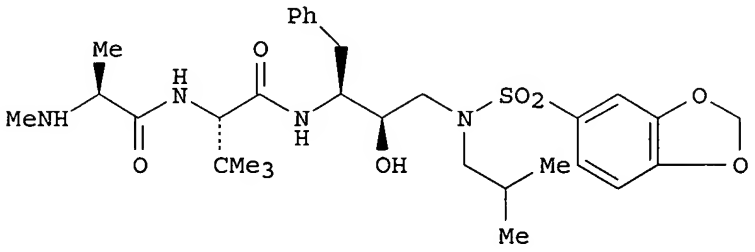

I

AB R13R12NCR10R11CONHCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, CH2CH2CONH2, CMe2SMe, etc.; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioialkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylalkyl; R4 = aryl, heteroaryl, heterocyclyl, benzoheteroaryl; R10 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl aralkyl, heteroaralkyl, alkylthioalkyl, etc.; R12, R13 = H, alkyl, aralkyl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, aryl, heteroaryl; with provisos), were prepared as retroviral protease inhibitors. Thus, title compound (I), prepared by solution phase methods,

inhibited HIV protease with IC50 = 1 nM.

IT **143224-62-8P 160232-08-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bisamino acid hydroxyethylaminosulfonamide **retroviral protease inhibitors**)

L15 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 30 Oct 1996
ACCESSION NUMBER: 1996:637443 CAPLUS
DOCUMENT NUMBER: 125:329473
TITLE: Preparation of aminediol-containing peptide analogs as retroviral protease inhibitors
INVENTOR(S): Gordon, Eric M.; Barrish, Joel C.; Bisacchi, Gregory S.; Sun, Chong-qing; Tino, Joseph A.; Vite, Gregory D.; Zahler, Robert
PATENT ASSIGNEE(S): E. R. Squibb & Sons, Inc., USA
SOURCE: U.S., 219 pp., Cont.-in-part of U.S. Ser. No. 927,027, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5559256	A	19960924	US 1993-79978	19930625
AU 9341659	A1	19940127	AU 1993-41659	19930630
AU 677194	B2	19970417		
HU 67090	A2	19950130	HU 1993-2080	19930719
CA 2100894	AA	19940121	CA 1993-2100894	19930720
NO 9302620	A	19940121	NO 1993-2620	19930720
EP 580402	A2	19940126	EP 1993-305691	19930720
EP 580402	A3	19970305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ZA 9305243	A	19940217	ZA 1993-5243	19930720
CN 1085546	A	19940420	CN 1993-108954	19930720
JP 06206857	A2	19940726	JP 1993-201016	19930720
US 5760036	A	19980602	US 1995-455295	19950531
US 5776933	A	19980707	US 1995-456125	19950531

PRIORITY APPLN. INFO.: US 1992-916916 B2 19920720
US 1992-927027 B2 19920806
US 1993-79978 A 19930625

OTHER SOURCE(S): MARPAT 125:329473
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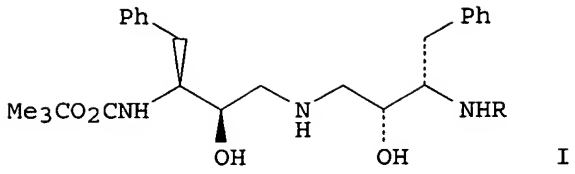

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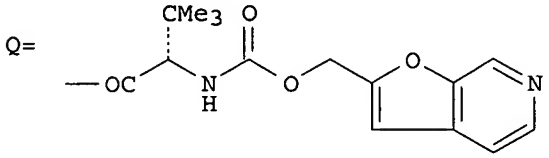

AB Aa-E-NR8CHR9H(OH)CH2NHCH2CH(OH)CHR9NR8-E-Ab [Aa, Ab = H, alkyl, R3C(:Z), R3SO2, R3R4NSO2, R3R4NC(:Z), R3SC(:O), R5R6R7COC(:Z); E = a single bond or a peptide chain containing 1 to 4 amino acids, the N-terminus of which is bonded to Aa or Ab; R3, R4 = H, alkyl, aryl, carbocyclyl; R5, R6, R7 = H, alkyl, aryl, carbocyclyl, fluorenyl, alkynyl, alkenyl; R5, R6, and R7 may, independently, be joined together with the carbon atom to which they are bonded, to form a mono-, bi- or tricyclic carbocyclic ring system; R8 = H, alkyl; R9 = arylalkyl; Z = O, S; wherein: wherever they appear alone or as part of another group, unless otherwise indicated, the terms "alkaline" or "alkyl" denote a straight or branched chain saturated radical containing 1 to 12 carbons in the normal chain, optionally substituted by one or more groups selected from (un)protected OH, oxo (with the proviso that the carbon bearing the oxo group is not adjacent to a heteroatom), CO2H, halo, alkoxy, aryloxy, alkoxycarbonyl, etc.] or salts thereof, which inhibit retroviral protease and are particularly useful in the treatment and/or prevention of HIV infection (AIDS), are prepared Thus, bis(3-amino-2-hydroxy-4-phenylbutyl)amine derivative (I; R = H) was condensed with L-tert-leucine derivative (HO-Q) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and HOBT in DMF/CH2CH2 at 0° to room temperature to give the title compound I (R = Q). The latter compound at 10 μM in vitro inhibited 99% HIV protease and showed IC50 of 0.012 μM which was the concentration of drug that increased the formazan production in CEM-SS cells infected with the RF strain of HIV to 50% of that produced by uninfected cells in the absence of drug.

IT **161302-38-1P 161302-39-2P 161302-40-5P**
162537-26-0P 162537-37-3P 162537-75-9P
162537-91-9P 162537-98-6P 162538-11-6P
162538-12-7P 162538-13-8P 162538-14-9P
162538-15-0P 162538-18-3P 162538-19-4P
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162541-02-8P 162541-03-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminediol-containing peptide analogs as **retroviral protease inhibitors** for treatment of HIV infection (AIDS))

IT **162541-04-0P 162541-05-1P 162541-06-2P**
162541-07-3P 162541-08-4P 162541-09-5P
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183255-94-9P 183256-02-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminediol-containing peptide analogs as **retroviral protease inhibitors** for treatment of HIV infection (AIDS))

IT **143576-95-8P 160232-54-2P 162536-41-6P**
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162537-35-1P 162537-36-2P 162537-39-5P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminediol-containing peptide analogs as **retroviral protease inhibitors** for treatment of HIV infection (AIDS))

L15 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 20 Sep 1996
ACCESSION NUMBER: 1996:560529 CAPLUS
DOCUMENT NUMBER: 125:221368
TITLE: Method of preparing retroviral protease inhibitor intermediates via diastereomer purification
INVENTOR(S): Ng, John S.; Przybyla, Claire A.; Zhang, Shu-Hong
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622275	A1	19960725	WO 1996-US918	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 5831117	A	19981103	US 1995-376340	19950120
CA 2210973	AA	19960725	CA 1996-2210973	19960118
AU 9647653	A1	19960807	AU 1996-47653	19960118
AU 692062	B2	19980528		
BR 9606981	A	19971104	BR 1996-6981	19960118
EP 804410	A1	19971105	EP 1996-903641	19960118
EP 804410	B1	20010829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
CN 1177955	A	19980401	CN 1996-192444	19960118
JP 10512571	T2	19981202	JP 1996-522442	19960118
AT 204851	E	20010915	AT 1996-903641	19960118
ES 2162650	T3	20020101	ES 1996-903641	19960118
PT 804410	T	20020130	PT 1996-903641	19960118
CN 1623977	A	20050608	CN 2004-10056028	19960118
US 6201150	B1	20010313	US 1998-24662	19980217

US 2001047111	A1	20011129	US 2000-741087	20001221
US 6515162	B2	20030204		
US 2003171612	A1	20030911	US 2002-325952	20021223
US 2005131075	A1	20050616	US 2004-961405	20041012
US 7060851	B2	20060613		

PRIORITY APPLN. INFO.:

US 1995-376340 A 19950120

WO 1996-US918 W 19960118

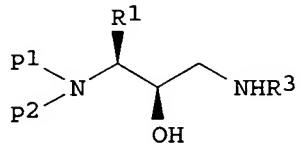
US 1998-24662 A1 19980217

US 2000-741087 A1 20001221

US 2002-325952 A1 20021223

OTHER SOURCE(S): MARPAT 125:221368

GI



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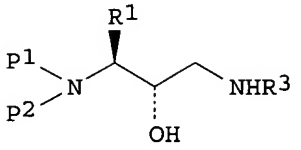

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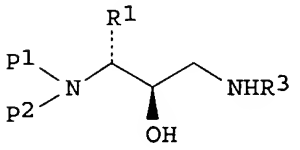

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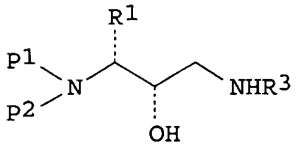


IV

AB The title compds. [I-IV; P1, P2 = H, acyl, aralkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, , etc.; R1 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, (un)substituted aralkyl; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, heteroaryl, aryl, etc.], useful as pharmaceutical intermediates (no data), are prepared and crystallized from solution in the form of a salt (i.e., organic acid and inorg. acid salts of the amine intermediates). The method is suitable for large-scale (i.e., multi-kilogram) production

IT **160232-08-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of preparing **retroviral protease inhibitor** intermediates via diastereomer purification)

L15 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Nov 1995
ACCESSION NUMBER: 1995:921865 CAPLUS
DOCUMENT NUMBER: 123:339376
TITLE: Preparation of diaminoalcohols as retroviral protease inhibitor intermediates
INVENTOR(S): Ng, John S.; Przybyla, Claire A.; Mueller, Richard A.; Vasquez, Michael L.; Getman, Daniel P.; Freskos, John J.; Decrescenzo, Gary A.; Bertenshaw, Deborah E.; Heintz, Robert M.; et al.

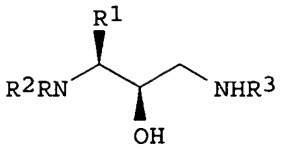
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; et al.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514653	A1	19950601	WO 1994-US12201	19941031
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9510833	A1	19950613	AU 1995-10833	19941031
EP 730570	A1	19960911	EP 1995-901697	19941031
EP 730570	B1	20000419		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 855388	A2	19980729	EP 1998-103779	19941031
EP 855388	A3	19990714		
EP 855388	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 191907	E	20000515	AT 1995-901697	19941031
ES 2145252	T3	20000701	ES 1995-901697	19941031
PT 730570	T	20001031	PT 1995-901697	19941031
AT 214046	E	20020315	AT 1998-103779	19941031
PT 855388	T	20020731	PT 1998-103779	19941031
ES 2173520	T3	20021016	ES 1998-103779	19941031
US 5648511	A	19970715	US 1995-452187	19950525
US 5872298	A	19990216	US 1997-833737	19970409
US 5872299	A	19990216	US 1997-854133	19970508
GR 3033429	T3	20000929	GR 2000-401119	20000516

PRIORITY APPLN. INFO.:

US 1993-156498	A1	19931123
US 1990-615210	B2	19901119
US 1991-789646	B2	19911114
US 1992-886558	B2	19920520
EP 1995-901697	A3	19941031
WO 1994-US12201	W	19941031
US 1995-452187	A1	19950525

OTHER SOURCE(S): MARPAT 123:339376
GI



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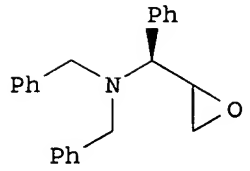

II

AB Title compds. [I; R, R2 = acyl, aralkyl, alkoxycarbonyl, etc.; R2RN = heterocyclyl; R1 = (cyclo)alkyl, aryl(alkyl), etc.; R3 = H, (cyclo)alkyl, aryl(alkyl), etc.] were prepared Thus, L-phenylalanine was N,N-diprotected and the product reduced to the aminoalc. which was oxidized to give (S)-PhCH2CH[N(CH2PH)2]CHO. The latter was treated with ICH2CL and BuLi in THF at <25° to give an 86:14 mixture of oxiranes (2R)- and (2S)-II the latter of which was condensed with Me2CHCH2NH2 to give I (R = R2 = CH2Ph, R1 = Ph, R3 = CH2CHMe2).

IT **160232-08-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diaminoalcs. as **retroviral protease inhibitor** intermediates)

L15 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 May 1994
ACCESSION NUMBER: 1994:271184 CAPLUS
DOCUMENT NUMBER: 120:271184
TITLE: Preparation of trifluoromethyl pseudopeptides active against retroviruses
INVENTOR(S): Haebich, Dieter; Roeben, Wolfgang; Hansen, Jutta; Paessens, Arnold
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 65 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4126485	A1	19930211	DE 1991-4126485	19910810
US 5430151	A	19950704	US 1992-920216	19920724
EP 528242	A2	19930224	EP 1992-113173	19920803
EP 528242	A3	19930602		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2075547	AA	19930211	CA 1992-2075547	19920807
JP 05294916	A2	19931109	JP 1992-233014	19920807
US 5605926	A	19970225	US 1995-419294	19950410

PRIORITY APPLN. INFO.: DE 1991-4126485 A 19910810
US 1992-920216 A3 19920724

OTHER SOURCE(S): MARPAT 120:271184
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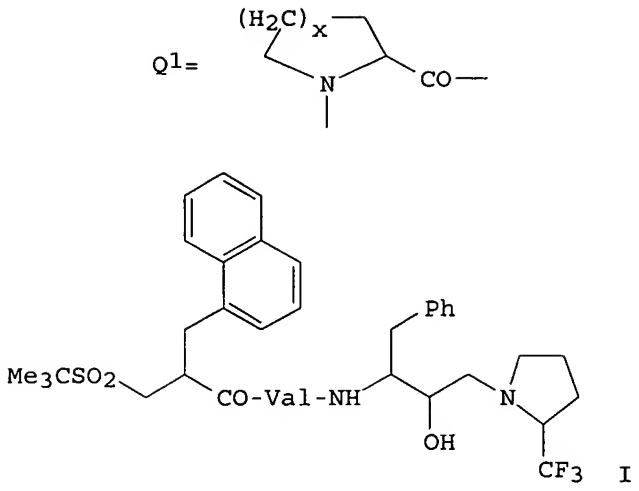

I

AB WABDNHCHR1ECH2NR2CHR3CF3 [W = H, protecting group, (aryl-substituted) alkyl alkenyl, acyl; A, B, D = bond, NHCMe2(CH2)rCO, Q1, NR14CHR15(CH2)zO; r, z = 0, 1; x = 1, 2; R14 = H, alkyl; R15 = H, cycloalkyl, aryl, (substituted) alkyl; R1 = (substituted) alkyl, alkenyl; E = CH(OH), CH(OH)CH(OH); R2, R3 = H, alkyl; R2R3 = atoms to complete a (substituted) (anellated) heterocyclic ring], were prepared Thus, title compound (I), prepared by solution phase methods starting with BOC-Val-OH via BOC-Val-NHCH(CH:CH2)CH2Ph, inhibited syncytia formation induced by HIV in lymphocytes with IC50 = 0.14 μM.

IT **154630-52-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as **retroviral protease inhibitor**)

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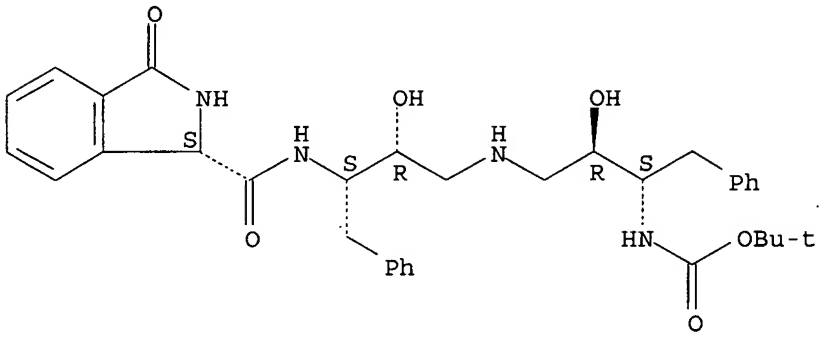
162539-13-1/BI OR 162539-15-3/BI OR 162

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Carbamic acid, [3-[[3-[[(2,3-dihydro-3-oxo-1H-isoindol-1-yl)carbonyl]amino]-2-hydroxy-4-phenylbutyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester, [1S-[1R*[1(1R*,2S*),2S*,3R*]]]- (9CI)
MF C34 H42 N4 O6

Absolute stereochemistry.

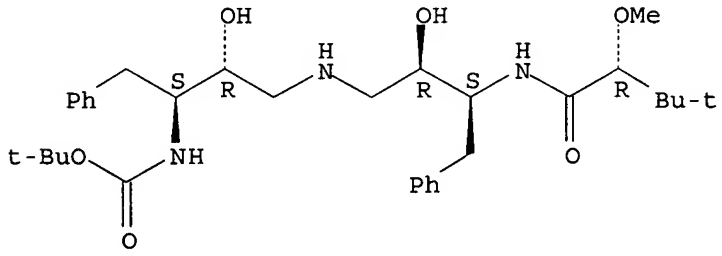


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):24

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Oxa-5,9,13-triazatetradecan-14-oic acid, 3-(1,1-dimethylethyl)-7,11-dihydroxy-4-oxo-6,12-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3R-(3R*,6S*,7R*,11R*,12S*)]- (9CI)
MF C32 H49 N3 O6

Absolute stereochemistry.



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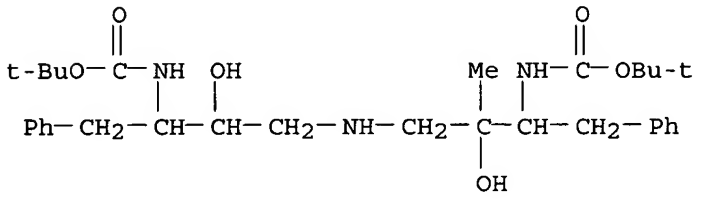
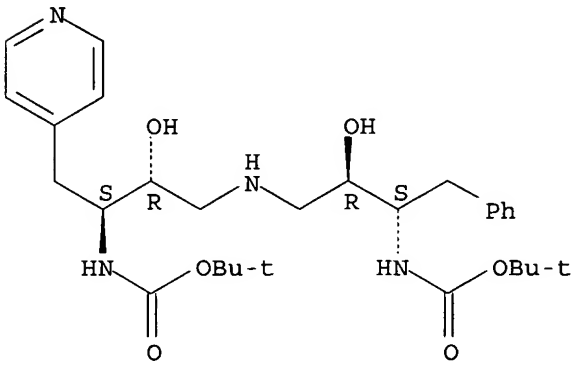
L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-4,13,13-trimethyl-11-oxo-3,9-bis(phenylmethyl)-, 1,1-dimethylethyl ester (9CI)
MF C31 H47 N3 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-11-oxo-3-(phenylmethyl)-9-(4-pyridinylmethyl)-, 1,1-dimethylethyl ester, (3S,4R,8R,9S)- (9CI)
MF C29 H44 N4 O6

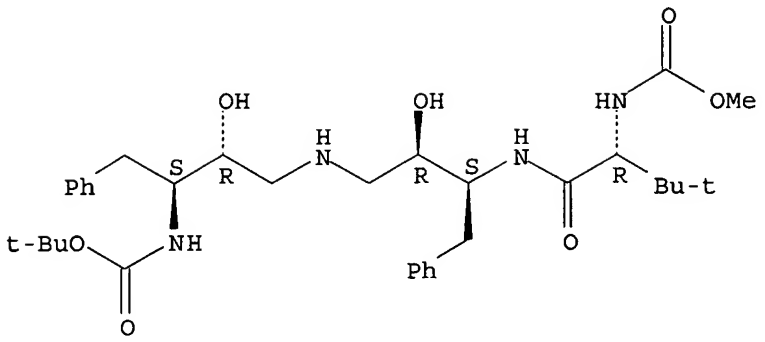
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,5,9,13-Tetraazatetradecanedioic acid, 3-(1,1-dimethylethyl)-7,11-dihydroxy-4-oxo-6,12-bis(phenylmethyl)-, 14-(1,1-dimethylethyl) 1-methyl ester, [3R-(3R*,6S*,7R*,11R*,12S*)]- (9CI)
MF C33 H50 N4 O7

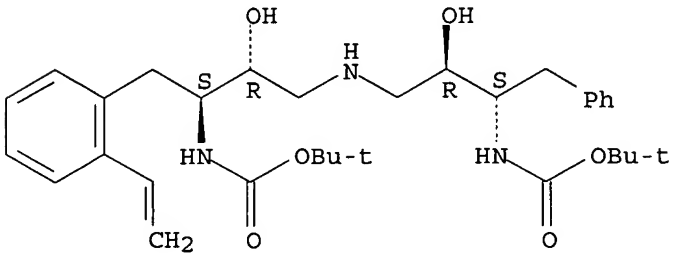
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 3-[(2-ethenylphenyl)methyl]-4,8-dihydroxy-13,13-dimethyl-11-oxo-9-(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3R*,4S*,8S*,9R*)]- (9CI)
MF C32 H47 N3 O6

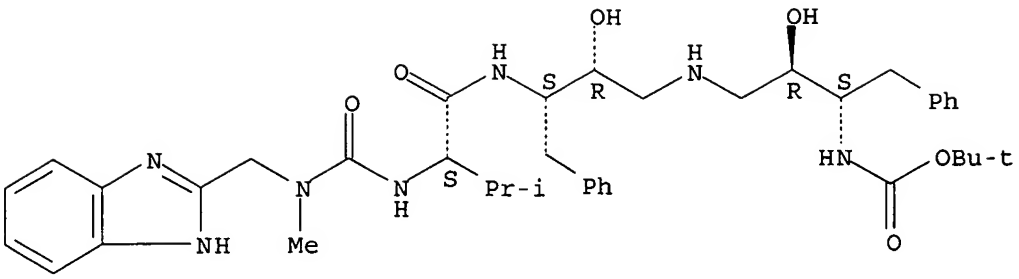
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,4,7,11,15-Pentaazahexadecanoic acid, 1-(1H-benzimidazol-2-yl)-9,13-dihydroxy-2-methyl-5-(1-methylethyl)-3,6-dioxo-8,14-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [5S-(5R*,8R*,9S*,13S*,14R*)]- (9CI)
MF C40 H55 N7 O6

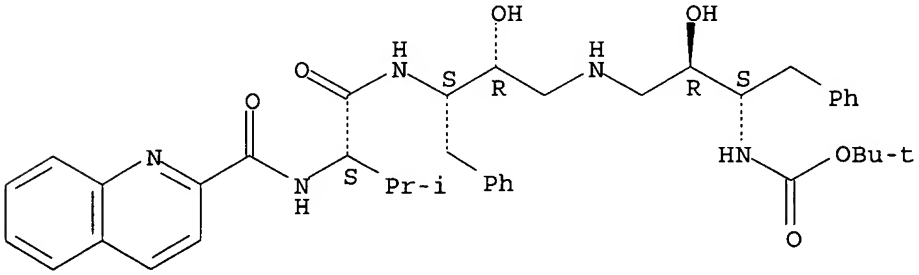
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,5,9,13-Tetraazatetradecan-14-oic acid, 7,11-dihydroxy-3-(1-methylethyl)-1,4-dioxo-6,12-bis(phenylmethyl)-1-(2-quinolinyl)-, 1,1-dimethylethyl ester, [3S-(3R*,6R*,7S*,11S*,12R*)]- (9CI)
MF C40 H51 N5 O6

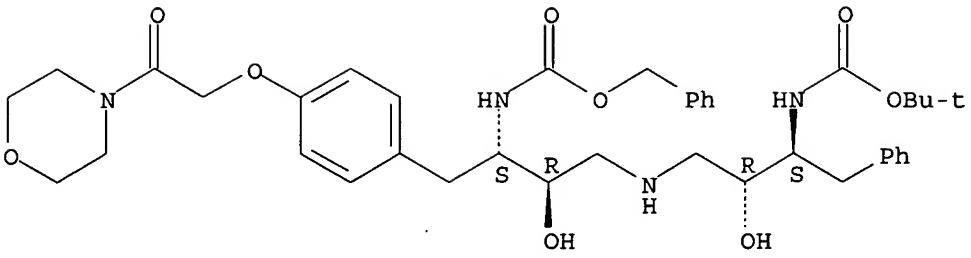
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-3-[[4-[2-(4-morpholinyl)-2-oxoethoxy]phenyl]methyl]-11-oxo-9-(phenylmethyl)-, phenylmethyl ester, [3S-(3R*,4S*,8S*,9R*)]- (9CI)
MF C39 H52 N4 O9

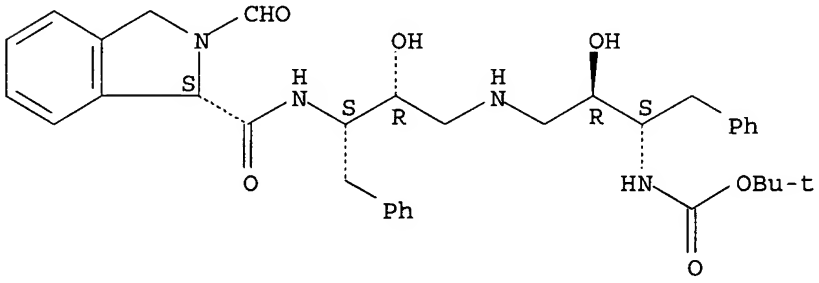
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Carbamic acid, [3-[[3-[[(2-formyl-2,3-dihydro-1H-isoindol-1-yl)carbonyl]amino]-2-hydroxy-4-phenylbutyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester, [1S-[1R*[1(1R*,2S*),2S*,3R*]]]- (9CI)
MF C35 H44 N4 O6

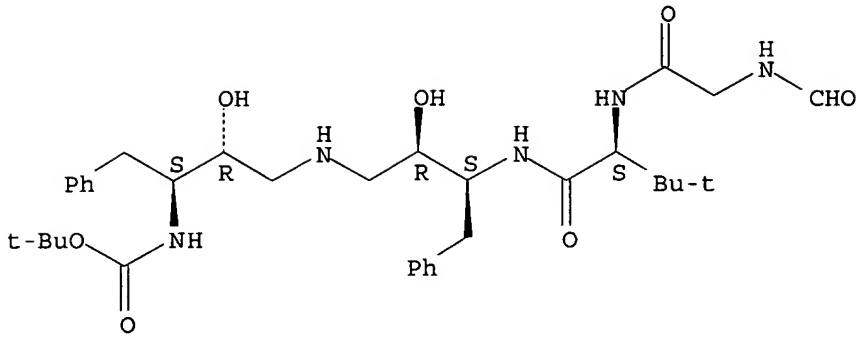
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN L-Valinamide, N-formylglycyl-N-[3-[[3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-methyl-, [2R-[1(1S*,2R*),2R*,3S*]]-(9CI)
MF C34 H51 N5 O7

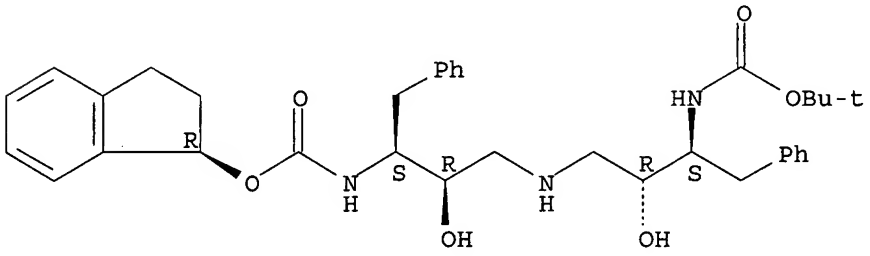
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-11-oxo-3,9-bis(phenylmethyl)-, 2,3-dihydro-1H-inden-1-yl ester, [1R-[1R*(3S*,4R*,8R*,9S*)]]- (9CI)
MF C35 H45 N3 O6

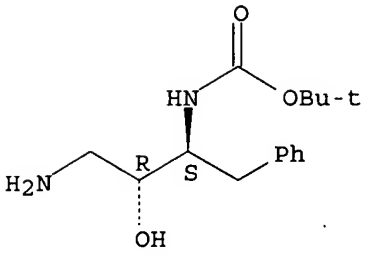
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Carbamic acid, [(1S,2R)-3-amino-2-hydroxy-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester (9CI)
MF C15 H24 N2 O3

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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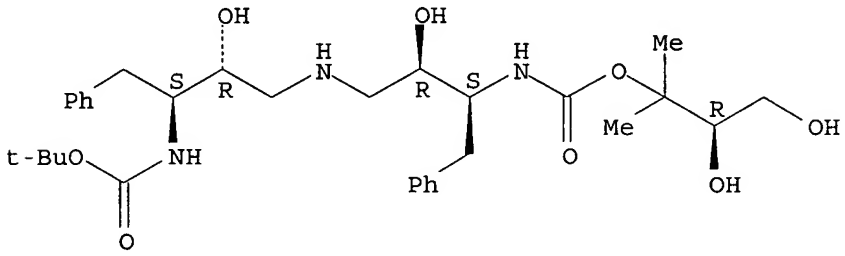
IN 12-Oxa-2,6,10-triazapentadecanoic acid, 4,8,14,15-tetrahydroxy-13,13-dimethyl-11-oxo-3,9-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3R*,4S*,8S*,9R*,14S*)]- (9CI)
MF C31 H47 N3 O8

Absolute stereochemistry.



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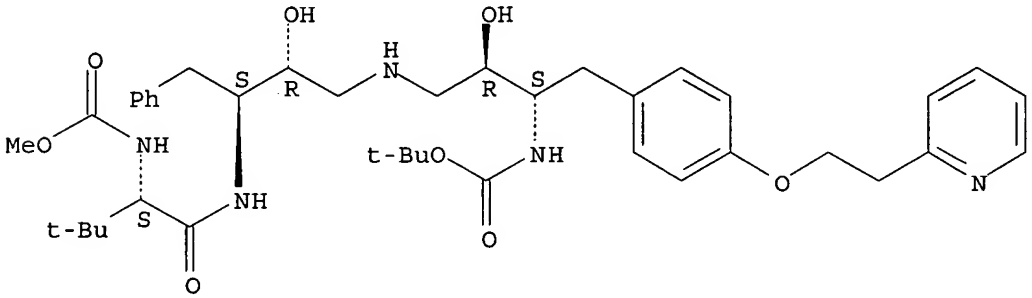
L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,5,9,13-Tetraazatetradecanedioic acid, 3-(1,1-dimethylethyl)-7,11-dihydroxy-4-oxo-6-(phenylmethyl)-12-[[4-[2-(2-pyridinyl)ethoxy]phenyl]methyl]-, 14-(1,1-dimethylethyl) 1-methyl ester, [3S-(3R*,6R*,7S*,11S*,12R*)]- (9CI)
MF C40 H57 N5 O8

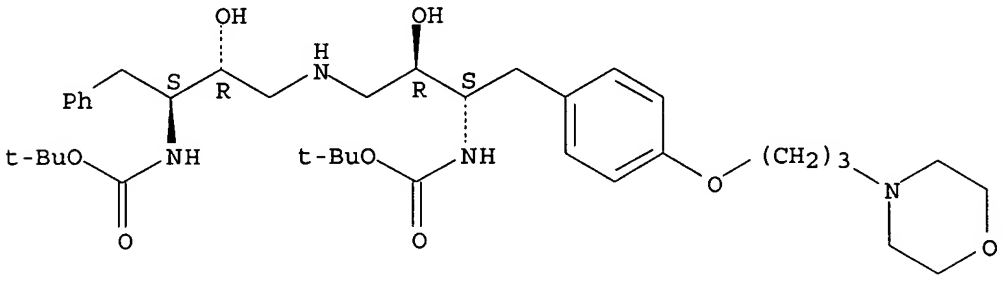
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-3-[[4-[3-(4-morpholinyl)propoxy]phenyl]methyl]-11-oxo-9-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,4R,8R,9S)- (9CI)
MF C37 H58 N4 O8

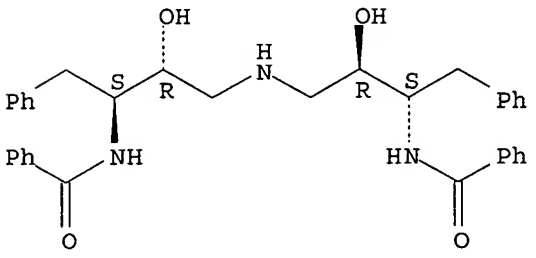
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, N,N'-[iminobis[2-hydroxy-1-(phenylmethyl)-3,1-propanediyl]]bis-, [1S-[1R*,2S*,3(1R*,2S*)]]- (9CI)
MF C34 H37 N3 O4

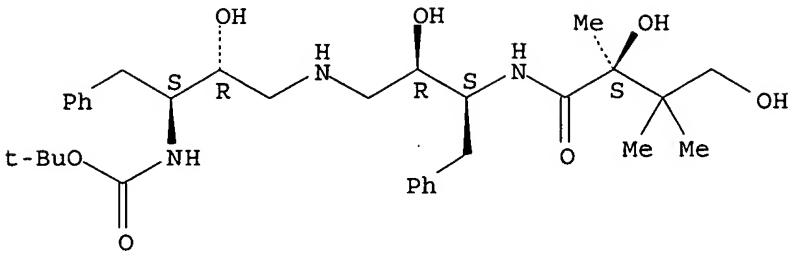
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Carbamic acid, [3-[[3-[(2,4-dihydroxy-2,3,3-trimethyl-1-oxobutyl)amino]-2-hydroxy-4-phenylbutyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester, [2R-[1(1S*,2R*),2R*,3S*(S*)]]- (9CI)
MF C32 H49 N3 O7

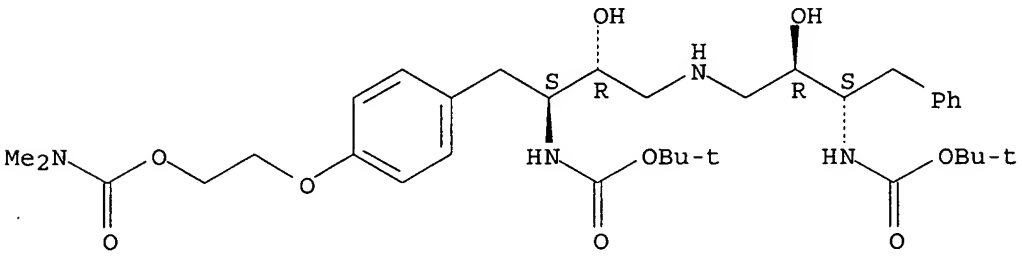
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 3-[[4-[2-[[(dimethylamino)carbonyl]oxy]ethoxy]phenyl]methyl]-4,8-dihydroxy-13,13-dimethyl-11-oxo-9-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,4R,8R,9S)- (9CI)
MF C35 H54 N4 O9

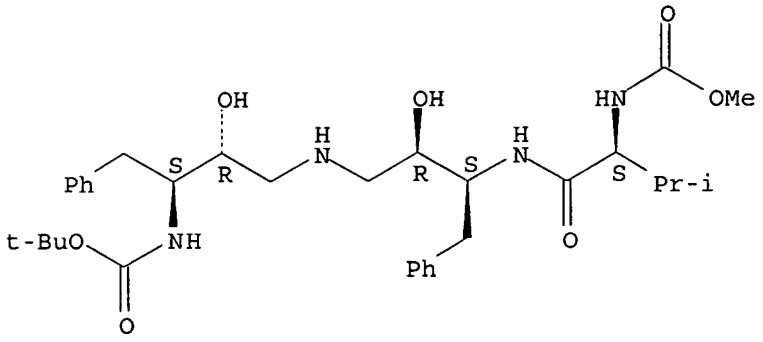
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,5,9,13-Tetraazatetradecanedioic acid, 7,11-dihydroxy-3-(1-methylethyl)-4-oxo-6,12-bis(phenylmethyl)-, 14-(1,1-dimethylethyl) 1-methyl ester, [3S-(3R*,6R*,7S*,11S*,12R*)]- (9CI)
MF C32 H48 N4 O7

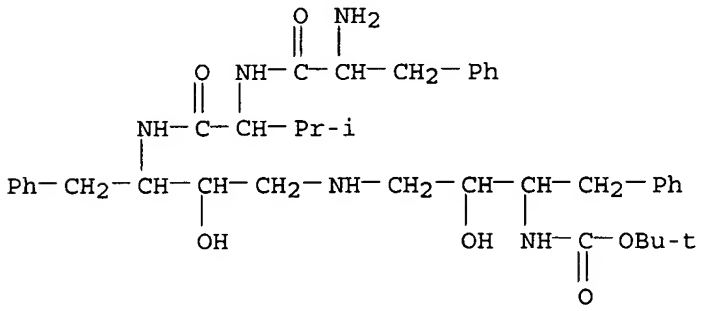
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

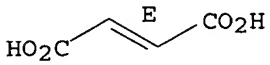
L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN L-Valinamide, L-phenylalanyl-N-[3-[[3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-, [2R-[1(1S*,2R*),2R*,3S*]]-, (2E)-2-butenedioate (2:3) (salt) (9CI)
MF C39 H55 N5 O6 . 3/2 C4 H4 O4

CM 1



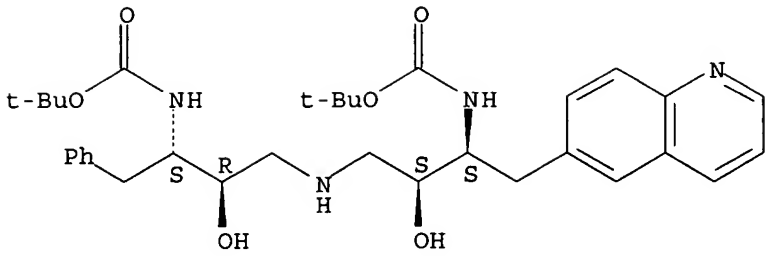
CM 2

Double bond geometry as shown.



L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-11-oxo-3-(phenylmethyl)-9-(6-quinolinylmethyl)-, 1,1-dimethylethyl ester, [3S-(3R*,4S*,8R*,9R*)]- (9CI)
MF C33 H46 N4 O6

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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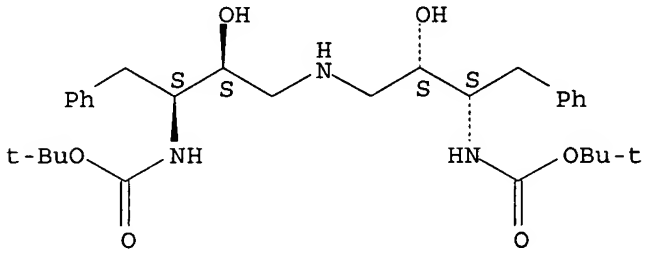
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-11-oxo-3,9-bis(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,4S,8S,9S)-(9CI)
MF C30 H45 N3 O6

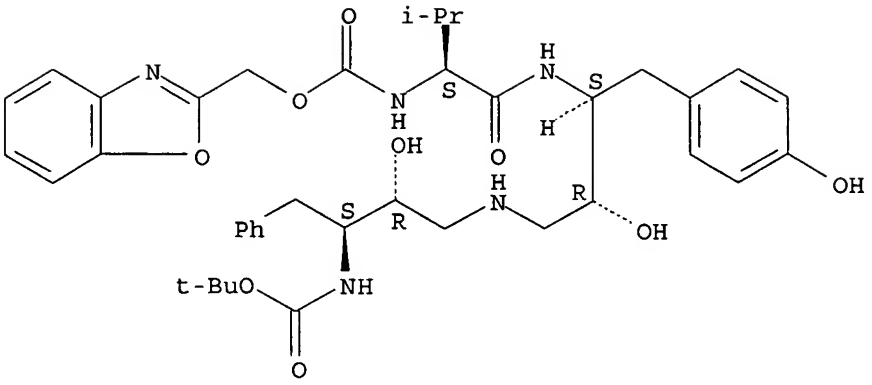
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2,5,9,13-Tetraazatetradecanedioic acid, 7,11-dihydroxy-6-[(4-hydroxyphenyl)methyl]-3-(1-methylethyl)-4-oxo-12-(phenylmethyl)-, 1-(2-benzoxazolylmethyl) 14-(1,1-dimethylethyl) ester, [3S-(3R*,6R*,7S*,11S*,12R*)]- (9CI)
MF C39 H51 N5 O9

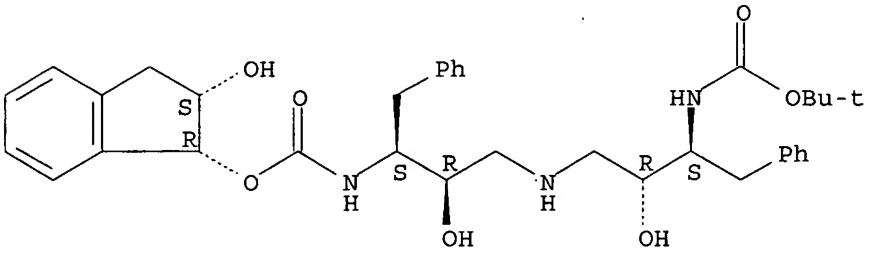
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L16 421 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 12-Oxa-2,6,10-triazatetradecanoic acid, 4,8-dihydroxy-13,13-dimethyl-11-oxo-3,9-bis(phenylmethyl)-, 2,3-dihydro-2-hydroxy-1H-inden-1-yl ester, [1R-[1α(3S*,4R*,8R*,9S*),2α]]- (9CI)
MF C35 H45 N3 O7

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

FILE 'CAOLD' ENTERED AT 16:34:53 ON 15 JUN 2006
L17 0 SEA ABB=ON PLU=ON L16

FILE 'USPATFULL' ENTERED AT 16:34:57 ON 15 JUN 2006
L18 171 SEA ABB=ON PLU=ON L16
L19 0 SEA ABB=ON PLU=ON L18(L)((RETROVIR? OR RETRO(W)(VIRUS OR VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A)INHIBIT?

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:35:26 ON 15 JUN 2006
L20 9 SEA ABB=ON PLU=ON L16
L21 0 SEA ABB=ON PLU=ON L20 AND ((RETROVIR? OR RETRO(W)(VIRUS OR VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A) INHIBIT?

Searcher : Shears 571-272-2528

FILE 'MARPAT' ENTERED AT 11:37:17 ON 14 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE CONTENT: 1961-PRESENT VOL 144 ISS 24 (20060609/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

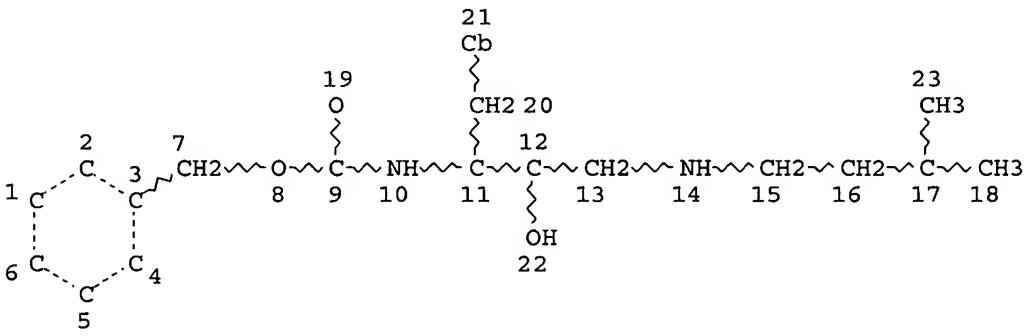
US 2006094872 04 MAY 2006
DE 102004047840 30 MAR 2006
EP 1640378 29 MAR 2006
JP 2006086284 30 MAR 2006
WO 2006045852 04 MAY 2006
GB 2416167 18 JAN 2006
FR 2875804 31 MAR 2006
RU 2272044 20 MAR 2006
CA 2518664 10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

L23 STR

Str. I



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 21
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L25 3 SEA FILE=MARPAT SSS FUL L23 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 10719 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.03

Searcher : Shears 571-272-2528

L25 ANSWER 1 OF 3 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:102190 MARPAT
TITLE: Preparation of substituted amines to treat Alzheimer's disease
INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 651 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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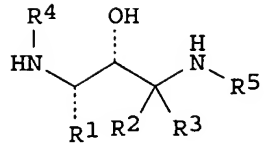
GI



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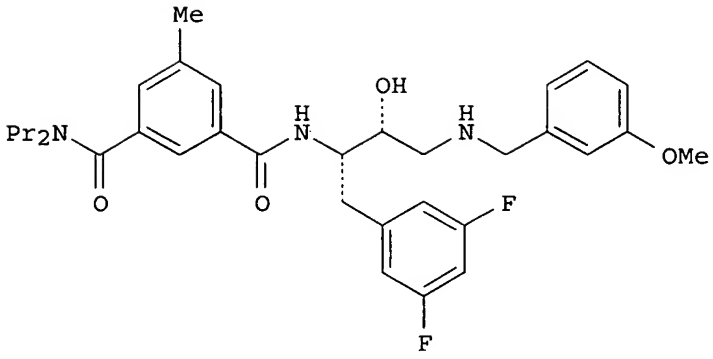

II

AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC50 of < 50 μM against beta-secretase.

L25 ANSWER 2 OF 3 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 127:50383 MARPAT

TITLE: Method of forming amino acid-derived diaminopropanols useful as chemical intermediates for protease inhibitors

INVENTOR(S): Pal, Biman; Ram, Siya; Cai, Bing; Sachdeva, Yesh P.; Shim, Jaechul; Zahr, Salah A.; Al-farhan, Emile; Gabriel, Richard L.

PATENT ASSIGNEE(S): Pharm-Eco Laboratories, Incorporated, USA

SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,475,138. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5631405	A	19970520	US 1995-472496	19950607
US 5475138	A	19951212	US 1994-271619	19940707
CA 2194480	AA	19960125	CA 1995-2194480	19950705

WO 9601788		A2	19960125	WO 1995-US8411	19950705
WO 9601788		A3	19960328		
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT		
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9530027		A1	19960209	AU 1995-30027	19950705
AU 693219		B2	19980625		
EP 769003		A1	19970423	EP 1995-926176	19950705
EP 769003		B1	20010516		
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EP 1059285		A2	20001213	EP 2000-202817	19950705
EP 1059285		A3	20011031		
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JP 2002515004		T2	20020521	JP 1996-504370	19950705
PRIORITY APPLN. INFO.:				US 1994-271619	19940707
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				US 1995-487294	19950607
				US 1995-487296	19950607
				EP 1995-926176	19950705
				WO 1995-US8411	19950705

AB The present invention relates to a method of forming a 1,3-diamino-3-substituted-2-propanol chemical intermediate R1R2NCHR3CHOHCR4R5NHCR6R6 [R1 = amino protecting group; R2 = H, alkyl, etc.; R3 = side chain of a naturally occurring (substituted) amino acid; R4, R5 = H, alkyl, etc.; R6 = H, alkyl, etc.] from which various chems., such as selected protease-inhibitors and other drugs, as well as polymers, can be synthesized. This method includes (a) reacting a 1,3-diamino-2-propanol derivative with an aldehyde or ketone (to form an imino compound), (b) reacting said imino compound with an imino reducing agent.

L25 ANSWER 3 OF 3 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	125:221368 MARPAT
TITLE:	Method of preparing retroviral protease inhibitor intermediates via diastereomer purification
INVENTOR(S):	Ng, John S.; Przybyla, Claire A.; Zhang, Shu-Hong
PATENT ASSIGNEE(S):	G.D. Searle and Co., USA
SOURCE:	PCT Int. Appl., 86 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622275	A1	19960725	WO 1996-US918	19960118
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RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE			

US 5831117	A	19981103	US 1995-376340	19950120
CA 2210973	AA	19960725	CA 1996-2210973	19960118
AU 9647653	A1	19960807	AU 1996-47653	19960118
AU 692062	B2	19980528		
BR 9606981	A	19971104	BR 1996-6981	19960118
EP 804410	A1	19971105	EP 1996-903641	19960118
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JP 10512571	T2	19981202	JP 1996-522442	19960118
AT 204851	E	20010915	AT 1996-903641	19960118
ES 2162650	T3	20020101	ES 1996-903641	19960118
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CN 1623977	A	20050608	CN 2004-10056028	19960118
US 6201150	B1	20010313	US 1998-24662	19980217
US 2001047111	A1	20011129	US 2000-741087	20001221
US 6515162	B2	20030204		
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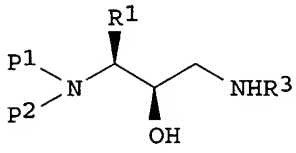

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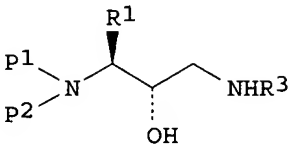

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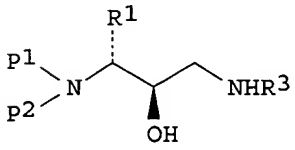

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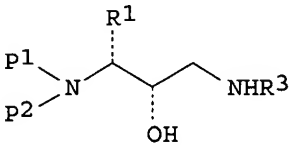

IV

AB The title compds. [I-IV; P1, P2 = H, acyl, aralkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, , etc.; R1 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, (un)substituted aralkyl; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, heteroaryl, aryl, etc.], useful as pharmaceutical intermediates (no data), are prepared and crystallized from solution in the form of a salt (i.e., organic acid and inorg. acid salts of the amine intermediates). The method is suitable for large-scale (i.e., multi-kilogram) production

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L22            0 SEA ABB=ON  PLU=ON  (?BENZYLOXY?(L)?ISOAMYLAMINE?)/CNS

     FILE 'HCAPLUS' ENTERED AT 17:16:54 ON 15 JUN 2006
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                 (BENZYL OR BZ)(W)OXY)(W)CARBONYL? OR BENZYLOXY CARBONYL?)(S
                 )(ISOAMYLAMINE OR (ISO OR I)(W)(AMYLAMINE OR AMYL AMINE)
                 OR ISOAMYL AMINE)
L24            0 SEA ABB=ON  PLU=ON  L23 NOT (L3 OR L15)

FILE 'MEDLINE' ENTERED AT 17:19:17 ON 15 JUN 2006

FILE 'BIOSIS' ENTERED AT 17:19:17 ON 15 JUN 2006
Copyright (c) 2006 The Thomson Corporation

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FILE 'SCISEARCH' ENTERED AT 17:19:17 ON 15 JUN 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'JICST-EPLUS' ENTERED AT 17:19:17 ON 15 JUN 2006
COPYRIGHT (C) 2006 Japan Science and Technology Agency (JST)

FILE 'JAPIO' ENTERED AT 17:19:17 ON 15 JUN 2006
COPYRIGHT (C) 2006 Japanese Patent Office (JPO)- JAPIO

L25            0 S L23

FILE 'HOME' ENTERED AT 17:19:42 ON 15 JUN 2006
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=> d que stat l2; d que stat l11; d his ful
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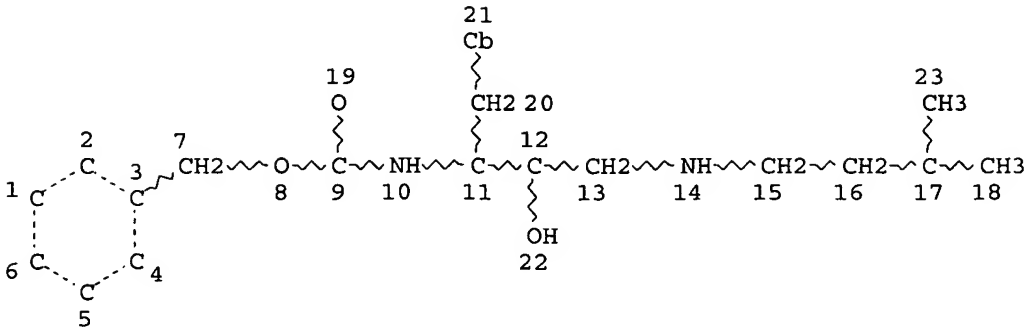

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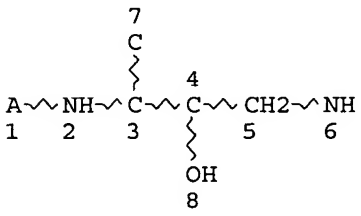

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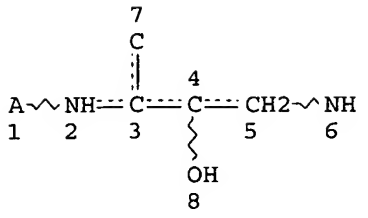

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ACT NAGUBAN1/A

L1 STR
L2 2 SEA SSS FUL L1

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D QUE STAT

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L*** DEL 107 S L5 AND ((RETROVIR? OR RETRO(W)(VIRUS OR VIRID? OR VIRAL?)

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L7 0 SEA ABB=ON PLU=ON L2

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ACT NAGUBAN2/A

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                  D QUE STAT L2
                  D QUE STAT L11
                  D COST

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                  )(ISOAMYLAMINE OR (ISO OR I)(W)(AMYLAMINE OR AMYL AMINE)
                  OR ISOAMYL AMINE)
L24             0 SEA ABB=ON  PLU=ON  L23 NOT (L3 OR L15)

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L25             0 SEA ABB=ON  PLU=ON  L23
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FILE 'HOME' ENTERED AT 17:19:42 ON 15 JUN 2006

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JUN 2006 HIGHEST RN 887828-19-5
DICTIONARY FILE UPDATES: 14 JUN 2006 HIGHEST RN 887828-19-5

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
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Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE CAPLUS

FILE COVERS 1907 - 15 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 14 Jun 2006 (20060614/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply They are available for your review at:

http://www.cas.org/infopolicy.html

FILE CAOLD
FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Jun 2006 (20060615/PD)
FILE LAST UPDATED: 15 Jun 2006 (20060615/ED)
HIGHEST GRANTED PATENT NUMBER: US7062785
HIGHEST APPLICATION PUBLICATION NUMBER: US2006130207
CA INDEXING IS CURRENT THROUGH 15 Jun 2006 (20060615/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jun 2006 (20060615/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE MEDLINE
FILE LAST UPDATED: 14 JUN 2006 (20060614/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 June 2006 (20060614/ED)

FILE EMBASE
FILE COVERS 1974 TO 15 Jun 2006 (20060615/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE HCAPLUS

FILE COVERS 1907 - 15 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 14 Jun 2006 (20060614/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 12 JUN 2006 <20060612/UP>
MOST RECENT DERWENT UPDATE: 200637 <200637/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html a
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS INDEX ENHANCEMENTS PLEASE VISIT:
http://www.scientific.thomson.com/cm/dwpienhancements <<<

FILE CONFSCI
FILE COVERS 1973 TO 10 Apr 2006 (20060410/ED)

CSA has resumed updates, see NEWS FILE

FILE SCISEARCH

FILE COVERS 1974 TO 8 Jun 2006 (20060608/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 14 JUN 2006 (20060614/ED)

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=> d his ful

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L1             STR
L2           2 SEA SSS FUL L1
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     FILE 'REGISTRY' ENTERED AT 16:24:46 ON 15 JUN 2006
               D QUE STAT

     FILE 'CAPLUS' ENTERED AT 16:24:46 ON 15 JUN 2006
L3          42 SEA ABB=ON  PLU=ON  L2
               D L3 1-42 IBIB ABS HITSTR

     FILE 'CAOLD' ENTERED AT 16:25:20 ON 15 JUN 2006
L4           0 SEA ABB=ON  PLU=ON  L2

     FILE 'USPATFULL' ENTERED AT 16:28:01 ON 15 JUN 2006
L5         109 SEA ABB=ON  PLU=ON  L2
L6           0 SEA ABB=ON  PLU=ON  L5(L)((RETROVIR? OR RETRO(W)(VIRUS OR
               VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A)INHIBIT?
L*** DEL    107 S L5 AND ((RETROVIR? OR RETRO(W)(VIRUS OR VIRID? OR VIRAL?)

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:28:57 ON 15 JUN 2006
L7           0 SEA ABB=ON  PLU=ON  L2

     FILE 'REGISTRY' ENTERED AT 16:29:04 ON 15 JUN 2006
               ACT NAGUBAN2/A
               ---------
L8             STR
L9          8394 SEA SSS FUL L8
               ---------
               D QUE
L10            STR L8
L11         8394 SEA SUB=L9 SSS FUL L10
               D QUE STAT

     FILE 'CAPLUS' ENTERED AT 16:31:41 ON 15 JUN 2006
L12          381 SEA ABB=ON  PLU=ON  L11
L13           50 SEA ABB=ON  PLU=ON  L12 AND ((RETROVIR? OR RETRO(W)(VIRUS
               OR VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A)INHIBI
               T?
L14           44 SEA ABB=ON  PLU=ON  L12(L)((RETROVIR? OR RETRO(W)(VIRUS OR
               VIRID? OR VIRAL?))(W)(PROTEASE OR PROTEINASE))(5A)INHIBIT?
L15           12 SEA ABB=ON  PLU=ON  L14 NOT L3
               SEL HIT L15 1-12 RN
               D L15 1-12 .BEVSTR

     FILE 'REGISTRY' ENTERED AT 16:33:40 ON 15 JUN 2006
L16          421 SEA ABB=ON  PLU=ON  (160232-08-6/BI OR 143224-62-8/BI OR
               161302-40-5/BI OR 143576-95-8/BI OR 154630-52-1/BI OR
               160232-54-2/BI OR 161302-38-1/BI OR 161302-39-2/BI OR
               162536-41-6/BI OR 162536-42-7/BI OR 162536-81-4/BI OR
               162537-12-4/BI OR 162537-26-0/BI OR 162537-35-1/BI OR
               162537-36-2/BI OR 162537-37-3/BI OR 162537-39-5/BI OR
```

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

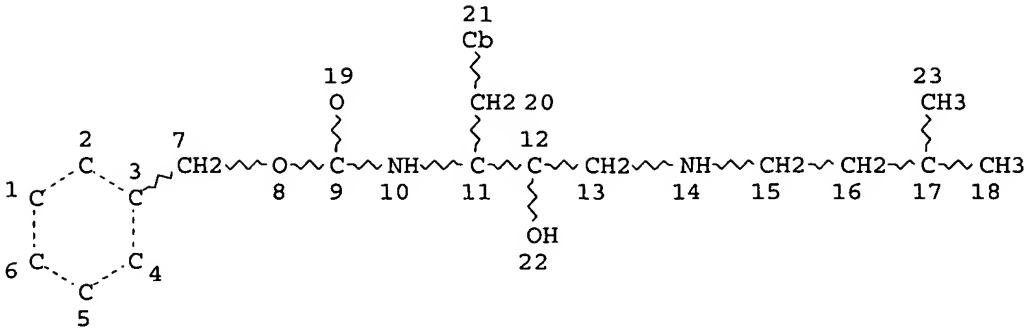
FILE JAPIO
FILE LAST UPDATED: 3 APR 2006 <20060403/UP>
FILE COVERS APRIL 1973 TO DECEMBER 22, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE. USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION ABOUT THE IPC REFORM <<<

FILE HOME

L23 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 21
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L25 3 SEA FILE=MARPAT SSS FUL L23 (MODIFIED ATTRIBUTES)

FILE 'REGISTRY' ENTERED AT 11:32:43 ON 14 JUN 2006
L19 0 SEA ABB=ON PLU=ON (?BENZYLOXY?(L)?ISOAMYLAMINE?)/CNS

FILE 'HCAPLUS' ENTERED AT 11:33:25 ON 14 JUN 2006
L*** DEL 0 S (BENZYLOXYCARBONYL? OR (BENZYLOXY OR (BENZYL OR BZ)(W)OXY
L20 1 SEA ABB=ON PLU=ON (BENZYLOXYCARBONYL? OR (BENZYLOXY OR (BENZYL OR BZ)(W)OXY)(W)CARBONYL? OR BENZYLOXY CARBONYL?)(S)(ISOAMYLAMINE OR (I OR ISO)(W)(AMYLAMINE OR AMYL AMINE) OR ISOAMYL AMINE)
L21 0 SEA ABB=ON PLU=ON L20 NOT L7

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:35:24 ON 14 JUN 2006
L22 0 SEA ABB=ON PLU=ON L20

FILE 'HOME' ENTERED AT 11:35:49 ON 14 JUN 2006

FILE 'MARPAT' ENTERED AT 11:36:06 ON 14 JUN 2006
D L1
L23 STR L1
L24 0 SEA SSS SAM L23 (MODIFIED ATTRIBUTES)
L25 3 SEA SSS FUL L23 (MODIFIED ATTRIBUTES)

FILE 'MARPAT' ENTERED AT 11:37:17 ON 14 JUN 2006
D QUE STAT L25
D L25 1-3 .BEVMAR1

Searcher : Shears 571-272-2528

FILE 'HOME' ENTERED AT 11:37:24 ON 14 JUN 2006
D QUE L2
D QUE L4
D QUE L25

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 JUN 2006 HIGHEST RN 887650-39-7
DICTIONARY FILE UPDATES: 13 JUN 2006 HIGHEST RN 887650-39-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE CAPLUS

FILE COVERS 1907 - 14 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 13 Jun 2006 (20060613/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply They are available for your review at:

http://www.cas.org/infopolicy.html

FILE CAOLD

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Jun 2006 (20060613/PD)
FILE LAST UPDATED: 13 Jun 2006 (20060613/ED)
HIGHEST GRANTED PATENT NUMBER: US7062785
HIGHEST APPLICATION PUBLICATION NUMBER: US2006123525
CA INDEXING IS CURRENT THROUGH 13 Jun 2006 (20060613/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Jun 2006 (20060613/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE MEDLINE
FILE LAST UPDATED: 13 JUN 2006 (20060613/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 7 June 2006 (20060607/ED)

FILE EMBASE
FILE COVERS 1974 TO 13 Jun 2006 (20060613/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE HCAPLUS

FILE COVERS 1907 - 14 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 13 Jun 2006 (20060613/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 12 JUN 2006 <20060612/UP>
MOST RECENT DERWENT UPDATE: 200637 <200637/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html a
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS INDEX ENHANCEMENTS PLEASE VISIT:
http://www.scientific.thomson.com/cm/dwpienhancements <<<

FILE CONFSCI
FILE COVERS 1973 TO 10 Apr 2006 (20060410/ED)

CSA has resumed updates, see NEWS FILE

FILE SCISEARCH

FILE COVERS 1974 TO 8 Jun 2006 (20060608/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS

FILE COVERS 1985 TO 14 JUN 2006 (20060614/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 3 APR 2006 <20060403/UP>
FILE COVERS APRIL 1973 TO DECEMBER 22, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE. USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION ABOUT THE IPC REFORM <<<

FILE HOME

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 144 ISS 24 (20060609/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

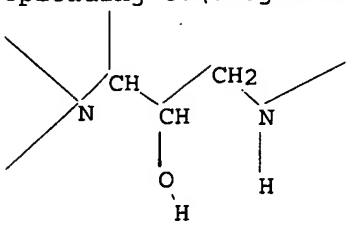
MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

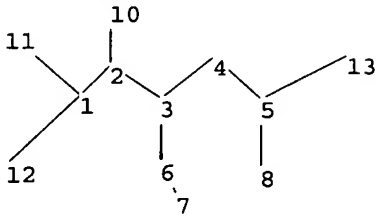
US	2006094872	04 MAY 2006
DE	102004047840	30 MAR 2006
EP	1640378	29 MAR 2006
JP	2006086284	30 MAR 2006
WO	2006045852	04 MAY 2006
GB	2416167	18 JAN 2006
FR	2875804	31 MAR 2006
RU	2272044	20 MAR 2006
CA	2518664	10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

=>
Uploading C:\Program Files\Stnexp\Queries\aminoalcoholC.str





chain nodes :
1 2 3 4 5 6 7 8 10 11 12 13
chain bonds :
1-2 1-11 1-12 2-3 2-10 3-4 3-6 4-5 5-8 5-13 6-7
exact/norm bonds :
1-2 1-11 1-12 3-6 5-13
exact bonds :
2-3 2-10 3-4 4-5 5-8 6-7

G1:X,Cb,Cy,Hy,Ak

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS

Stereo Bonds:

6-3 (Single Wedge).

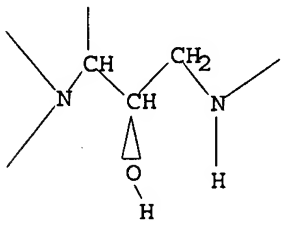
Stereo Chiral Centers:

3 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 3
L1 STRUCTURE UPLOADED

=> D L1
L1 HAS NO ANSWERS
L1 STR



G1 X,Cb,Cy,Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> S L1 SSS SAM
SAMPLE SEARCH INITIATED 12:15:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1035 TO ITERATE

100.0% PROCESSED 1035 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

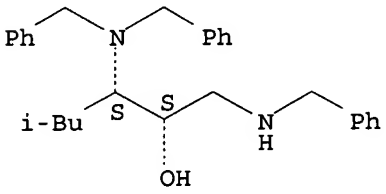
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 18770 TO 22630
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> D SCAN

L2 5 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Hexanol, 3-[bis(phenylmethyl)amino]-5-methyl-1-[(phenylmethyl)amino]-, (2S,3S)- (9CI)
MF C28 H36 N2 O

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

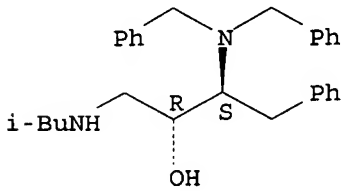
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1-5
'1-5' IS NOT VALID HERE

To display more answers, enter the number of answers you would like to see. To end the display, enter "NONE", "N", "0", or "END".
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

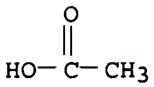
L2 5 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzenepropanol, β-[bis(phenylmethyl)amino]-α-[[(2-methylpropyl)amino]methyl]-, (αR,βS)-, monoacetate (salt) (9CI)
MF C28 H36 N2 O . C2 H4 O2

CM 1

Absolute stereochemistry.



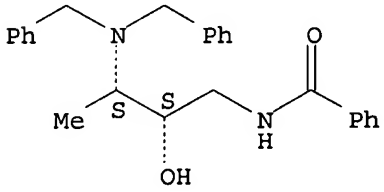
CM 2



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 5 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, N-[(2S,3S)-3-[bis(phenylmethyl)amino]-2-hydroxybutyl]- (9CI)
MF C25 H28 N2 O2

Absolute stereochemistry. Rotation (-).

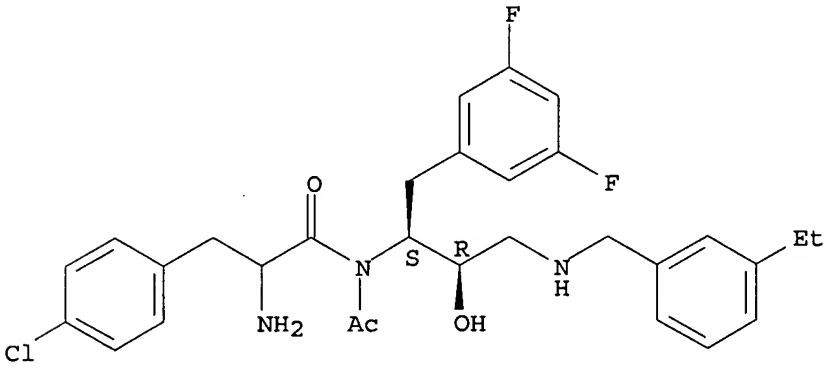


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 5 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzenepropanamide, N-acetyl-α-amino-4-chloro-N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]- (9CI)
MF C30 H34 Cl F2 N3 O3

Absolute stereochemistry.



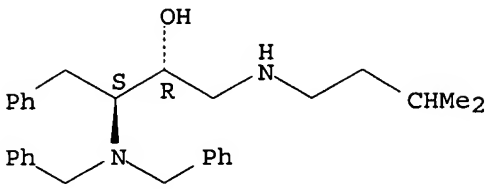
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 5 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzenepropanol, β-[bis(phenylmethyl)amino]-α-[[(3-methylbutyl)amino]methyl]-, [R-(R*,S*)]- (9CI)

MF C29 H38 N2 O

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.88	1.09

FILE 'CAPLUS' ENTERED AT 12:16:43 ON 19 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Jun 2006 VOL 144 ISS 26
FILE LAST UPDATED: 18 Jun 2006 (20060618/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> S ibib abs hitstr 1-
```
           15 IBIB
       227676 ABS
            0 HITSTR
      8704295 1
L3          0 IBIB ABS HITSTR 1-
              (IBIB(W)ABS(W)HITSTR(W)1)
```

=> D L2 1-5 iall
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

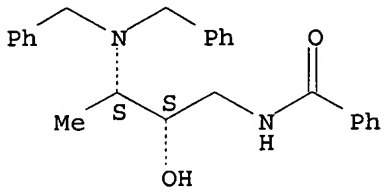
L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN

RN 865653-65-2 REGISTRY
ED Entered STN: 20 Oct 2005
CN Benzamide, N-[(2S,3S)-3-[bis(phenylmethyl)amino]-2-hydroxybutyl]- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C25 H28 N2 O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.18	3

Absolute stereochemistry. Rotation (-).



Experimental Properties (EPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Optical Rotatory Power (ORP)	-24.0 deg	Conc: 2.16 g/100mL Solv: chloroform (67-66-3) Temp: 25 deg C Wavlen: 589.3 nm	(1) CAS

(1) Concellon, Jose M.; Journal of Organic Chemistry 2005 V70(18) P7447-7450 CAPLUS

Experimental Property Tags (ETAG)

PROPERTY	NOTE
Carbon-13 NMR Spectra	(1) CAS
IR Absorption Spectra	(1) CAS
Mass Spectra	(1) CAS
Proton NMR Spectra	(1) CAS

(1) Concellon, Jose M.; Journal of Organic Chemistry 2005 V70(18) P7447-7450 CAPLUS

Predicted Properties (PPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	3.97	pH 1 25 deg C	(1)
Bioconc. Factor (BCF)	4.03	pH 2 25 deg C	(1)
Bioconc. Factor (BCF)	4.55	pH 3 25 deg C	(1)
Bioconc. Factor (BCF)	9.75	pH 4 25 deg C	(1)
Bioconc. Factor (BCF)	61.16	pH 5 25 deg C	(1)
Bioconc. Factor (BCF)	522.23	pH 6 25 deg C	(1)
Bioconc. Factor (BCF)	2681.09	pH 7 25 deg C	(1)
Bioconc. Factor (BCF)	4593.16	pH 8 25 deg C	(1)
Bioconc. Factor (BCF)	4946.01	pH 9 25 deg C	(1)
Bioconc. Factor (BCF)	4982.73	pH 10 25 deg C	(1)
Boiling Point (BP)	598.8+/-50.0 deg C	760 Torr	(1)
Density (DEN)	1.145+/-0.06 g/cm**3	760 Torr	(1)
Enthalpy of Vap. (HVAP)	93.77+/-3.0 kJ/mol	760 Torr	(1)
Flash Point (FP)	316.0+/-30.1 deg C		(1)
Freely Rotatable Bonds (FRB)	10		(1)
H acceptors (HAC)	4		(1)
H donors (HD)	2		(1)
Hydrogen Donors/Acceptors Sum (HDAS)	6		(1)
Koc (KOC)	12.28	pH 1 25 deg C	(1)
Koc (KOC)	12.45	pH 2 25 deg C	(1)
Koc (KOC)	14.06	pH 3 25 deg C	(1)
Koc (KOC)	30.15	pH 4 25 deg C	(1)
Koc (KOC)	189.16	pH 5 25 deg C	(1)
Koc (KOC)	1615.14	pH 6 25 deg C	(1)
Koc (KOC)	8291.96	pH 7 25 deg C	(1)
Koc (KOC)	14205.49	pH 8 25 deg C	(1)
Koc (KOC)	15296.78	pH 9 25 deg C	(1)
Koc (KOC)	15410.33	pH 10 25 deg C	(1)
logD (LOGD)	2.07	pH 1 25 deg C	(1)
logD (LOGD)	2.08	pH 2 25 deg C	(1)
logD (LOGD)	2.13	pH 3 25 deg C	(1)
logD (LOGD)	2.46	pH 4 25 deg C	(1)
logD (LOGD)	3.26	pH 5 25 deg C	(1)
logD (LOGD)	4.19	pH 6 25 deg C	(1)
logD (LOGD)	4.90	pH 7 25 deg C	(1)
logD (LOGD)	5.13	pH 8 25 deg C	(1)
logD (LOGD)	5.16	pH 9 25 deg C	(1)
logD (LOGD)	5.17	pH 10 25 deg C	(1)
logP (LOGP)	5.169+/-0.633	25 deg C	(1)
Mass Intrinsic Solubility (ISLB.MASS)	0.0012 g/L	25 deg C	(1)
Mass Solubility (SLB.MASS)	1.6 g/L	pH 1 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.5 g/L	pH 2 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.4 g/L	pH 3 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.62 g/L	pH 4 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.10 g/L	pH 5 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.012 g/L	pH 6 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0023 g/L	pH 7 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0013 g/L	pH 8 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0012 g/L	pH 9 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0012 g/L	pH 10 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0014 g/L	Unbuffered Water pH 7.73 25 deg C	(1)
Molar Intrinsic Solubility (ISLB.MOL)	0.0000032 mol/L	25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0040 mol/L	pH 1 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0039 mol/L	pH 2 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0035 mol/L	pH 3 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0016 mol/L	pH 4 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00026 mol/L	pH 5 25 deg C	(1)

Molar Solubility (SLB.MOL)	0.000030 mol/L	pH 6 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000059 mol/L	pH 7 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000034 mol/L	pH 8 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000032 mol/L	pH 9 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000032 mol/L	pH 10 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000037 mol/L	Unbuffered Water pH 7.73 25 deg C	(1)
Molar Volume (MVOL)	339.2+/-3.0 cm**3/mol	20 deg C 760 Torr	(1)
Molecular Weight (MW)	388.50		(1)
pKa (PKA)	13.96+/-0.20	Most Acidic 25 deg C	(1)
pKa (PKA)	6.94+/-0.50	Most Basic 25 deg C	(1)
Polar Surface Area (PSA)	52.57 A**2		(1)
Vapor Pressure (VP)	3.45E-15 Torr	25 deg C	(1)

This substance may exist in multiple tautomeric forms. The property values in this table are calculated based upon the displayed form and may therefore differ from experimental values based on the actual tautomeric ratio at equilibrium.

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.19 ((C) 1994-2006 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 143:346780 CA
TITLE: Regioselective Ring Opening of Amino Epoxides with Nitriles: An Easy Synthesis of (2R,3S)- and (2S,3S)-1,3-Diaminoalkan-2-ols with Differently Protected Amine Functions
AUTHOR(S): Concellon, Jose M.; Suarez, Jose Ramon; Del Solar, Virginia
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Facultad de Quimica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Journal of Organic Chemistry (2005), 70(18), 7447-7450
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 23-7 (Aliphatic Compounds)
Section cross-reference(s): 27

ABSTRACT:
Transformation of enantiopure (2R,1'S)- or (2S,1'S)-2-(1-aminoalkyl)epoxides into the corresponding (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols is described. The opening of the epoxide ring with different nitriles (Ritter reaction) takes place with total selectivity and in high yields in the presence of $BF_3 \cdot Et_2O$. Interestingly, the two amine groups are differently protected. A mechanism to explain this transformation is proposed.

SUPPL. TERM: regioselective ring opening amino epoxide nitrile; Ritter reaction amino epoxide nitrile; diamino alkanol prepn
INDEX TERM: Addition reaction
(Ritter; preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by regioselective ring opening of amino epoxides

with nitriles (Ritter reaction))
INDEX TERM: Epoxides
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amino; preparation of (2R,3S)- and
(2S,3S)-1,3-diaminoalkan-2-
ols by regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: Alcohols, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(amino; preparation of (2R,3S)- and
(2S,3S)-1,3-diaminoalkan-2-
ols by regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: Asymmetric synthesis and induction
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by
regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: Nitriles, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by
regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: Protective groups
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols
protected as dibenzylamine and acylamine)
INDEX TERM: Ring opening
(regioselective; preparation of (2R,3S)- and
(2S,3S)-1,3-diaminoalkan-2-ols by regioselective ring
opening of amino epoxides with nitriles (Ritter
reaction))
INDEX TERM: 75-05-8, Acetonitrile, reactions 78-82-0 100-47-0,
Benzonitrile, reactions 107-12-0, Propanenitrile
127927-41-7 127927-42-8 127927-43-9 127943-39-9
171815-93-3 171962-77-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by
regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: 865653-64-1P 865653-65-2P 865653-66-3P 865653-67-4P
865653-68-5P 865653-69-6P 865653-70-9P 865653-71-0P
865653-72-1P 865653-73-2P 865653-74-3P 865653-75-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by
regioselective ring opening of amino epoxides with
nitriles (Ritter reaction))
INDEX TERM: 109-63-7, Boron trifluoride etherate
ROLE: RGT (Reagent); RACT (Reactant or reagent)
(preparation of (2R,3S)- and (2S,3S)-1,3-diaminoalkan-2-ols by
regioselective ring opening of amino epoxides with
nitriles (Ritter reaction) in presence of boron
trifluoride etherate)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD.
REFERENCE(S): (1) Barluenga, J; J Chem Soc, Chem Commun 1994, P969 CAPLUS
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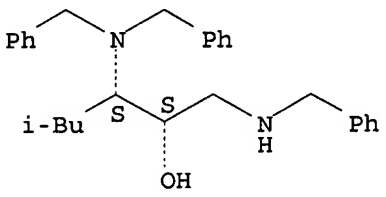
L2 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 591750-67-3 REGISTRY
ED Entered STN: 24 Sep 2003
CN 2-Hexanol, 3-[bis(phenylmethyl)amino]-5-methyl-1-[(phenylmethyl)amino]-, (2S,3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H36 N2 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.18	3

Absolute stereochemistry. Rotation (+).



Experimental Properties (EPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Optical Rotatory Power (ORP)	+2.6 deg	Conc: 0.71 g/100mL Solv: chloroform (67-66-3) Temp: 25 deg C Wavlen: 589.3 nm	(1) CAS

(1) Concellon, Jose M.; Journal of Organic Chemistry 2003 V68(16) P6407-6410 CAPLUS

Experimental Property Tags (ETAG)

PROPERTY	NOTE
Carbon-13 NMR Spectra	(1) CAS
IR Spectra	(1) CAS
Mass Spectra	(1) CAS
Proton NMR Spectra	(1) CAS

(1) Concellon, Jose M.; Journal of Organic Chemistry 2003 V68(16) P6407-6410 CAPLUS

Predicted Properties (PPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	31.94	pH 1 25 deg C	(1)
Bioconc. Factor (BCF)	31.95	pH 2 25 deg C	(1)
Bioconc. Factor (BCF)	32.01	pH 3 25 deg C	(1)
Bioconc. Factor (BCF)	32.68	pH 4 25 deg C	(1)
Bioconc. Factor (BCF)	42.24	pH 5 25 deg C	(1)
Bioconc. Factor (BCF)	371.83	pH 6 25 deg C	(1)
Bioconc. Factor (BCF)	10227.63	pH 7 25 deg C	(1)
Bioconc. Factor (BCF)	103362.91	pH 8 25 deg C	(1)
Bioconc. Factor (BCF)	313917.97	pH 9 25 deg C	(1)
Bioconc. Factor (BCF)	390540.62	pH 10 25 deg C	(1)
Boiling Point (BP)	565.0+/-50.0 deg C	760 Torr	(1)
Density (DEN)	1.067+/-0.06 g/cm**3	760 Torr	(1)
Enthalpy of Vap. (HVAP)	89.30+/-3.0 kJ/mol	760 Torr	(1)
Flash Point (FP)	295.5+/-30.1 deg C		(1)
Freely Rotatable Bonds (FRB)	13		(1)
H acceptors (HAC)	3		(1)
H donors (HD)	2		(1)
Hydrogen Donors/Acceptors Sum (HDAS)	5		(1)
Koc (KOC)	28.39	pH 1 25 deg C	(1)
Koc (KOC)	28.39	pH 2 25 deg C	(1)
Koc (KOC)	28.45	pH 3 25 deg C	(1)
Koc (KOC)	29.04	pH 4 25 deg C	(1)
Koc (KOC)	37.54	pH 5 25 deg C	(1)
Koc (KOC)	330.44	pH 6 25 deg C	(1)
Koc (KOC)	9089.02	pH 7 25 deg C	(1)
Koc (KOC)	91855.91	pH 8 25 deg C	(1)
Koc (KOC)	278970.38	pH 9 25 deg C	(1)
Koc (KOC)	347062.84	pH 10 25 deg C	(1)
logD (LOGD)	3.58	pH 1 25 deg C	(1)
logD (LOGD)	3.58	pH 2 25 deg C	(1)
logD (LOGD)	3.58	pH 3 25 deg C	(1)
logD (LOGD)	3.59	pH 4 25 deg C	(1)
logD (LOGD)	3.70	pH 5 25 deg C	(1)
logD (LOGD)	4.64	pH 6 25 deg C	(1)
logD (LOGD)	6.08	pH 7 25 deg C	(1)
logD (LOGD)	7.09	pH 8 25 deg C	(1)
logD (LOGD)	7.57	pH 9 25 deg C	(1)
logD (LOGD)	7.66	pH 10 25 deg C	(1)
logP (LOGP)	7.677+/-0.546	25 deg C	(1)
Mass Intrinsic Solubility (ISLB.MASS)	0.000096 g/L	25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 1 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 2 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 3 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 4 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.92 g/L	pH 5 25 deg C	(1)

Mass Solubility (SLB.MASS)	0.10 g/L	pH 6 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0037 g/L	pH 7 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00037 g/L	pH 8 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00012 g/L	pH 9 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.000100 g/L	pH 10 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00050 g/L	Unbuffered Water pH 7.86 25 deg C	(1)
Molar Intrinsic Solubility (ISLB.MOL)	0.00000023 mol/L	25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0029 mol/L	pH 1 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0029 mol/L	pH 2 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0029 mol/L	pH 3 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0028 mol/L	pH 4 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0022 mol/L	pH 5 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00025 mol/L	pH 6 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000090 mol/L	pH 7 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000089 mol/L	pH 8 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000029 mol/L	pH 9 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000024 mol/L	pH 10 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000012 mol/L	Unbuffered Water pH 7.86 25 deg C	(1)
Molar Volume (MVOL)	390.4+/-3.0 cm**3/mol	20 deg C 760 Torr	(1)
Molecular Weight (MW)	416.60		(1)
pKa (PKA)	14.11+/-0.20	Most Acidic 25 deg C	(1)
pKa (PKA)	8.43+/-0.29	Most Basic 25 deg C	(1)
Polar Surface Area (PSA)	35.50 A**2		(1)
Vapor Pressure (VP)	1.33E-13 Torr	25 deg C	(1)

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.19 ((C) 1994-2006 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 139:230328 CA
TITLE: Ring Opening of Nonactivated 2-(1-Aminoalkyl) Aziridines: Unusual Regio- and Stereoselective C-2 and C-3 Cleavage
AUTHOR(S): Concellon, Jose M.; Riego, Estela
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Facultad de Quimica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Journal of Organic Chemistry (2003), 68(16), 6407-6410 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 23-7 (Aliphatic Compounds)
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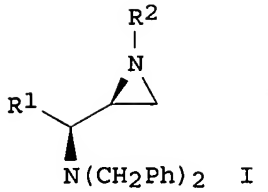

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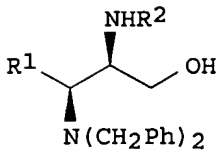
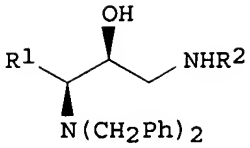


II



III

ABSTRACT:
The ring opening of nonactivated amino aziridines I (R1 = Me, Me2CHCH2, PhCH2, Me3CSiMe2OCH2; R2 = H2C:CHCH2, n-Pr, PhCH2) by water under acidic conditions has been investigated. Depending on the acid used, amino aziridines I were cleaved at C-3 or C-2 with high regioselectivity and total stereoselectivity, affording either chiral 2,3-diaminoalkan-1-ols II or 1,3-diaminoalkan-2-ols III in high yields.

SUPPL. TERM: aziridine aminoalkyl nonactivated regioselective stereoselective ring opening hydrolysis; alkanol diamino regioselective stereoselective prepn

INDEX TERM: Alcohols, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(amino; regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: Asymmetric synthesis and induction
(regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: Hydrolysis
Ring opening
(stereoselective, regioselective; regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: 127927-41-7
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(determination of absolute stereochem. of diamino alkanols; regio-
and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: 100-46-9, Benzyl amine, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(oxirane ring opening; regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: 341524-30-9 341524-32-1 341524-34-3 341524-35-4
341524-38-7 591750-70-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

INDEX TERM: 127927-57-5P 127927-58-6P 127927-60-0P 591750-59-3P
591750-61-7P 591750-63-9P 591750-64-0P 591750-65-1P

591750-66-2P 591750-67-3P 591750-68-4P 591750-69-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(regio- and stereoselective preparation of diamino alkanols via hydrolytic ring opening of nonactivated aminoalkyl aziridines)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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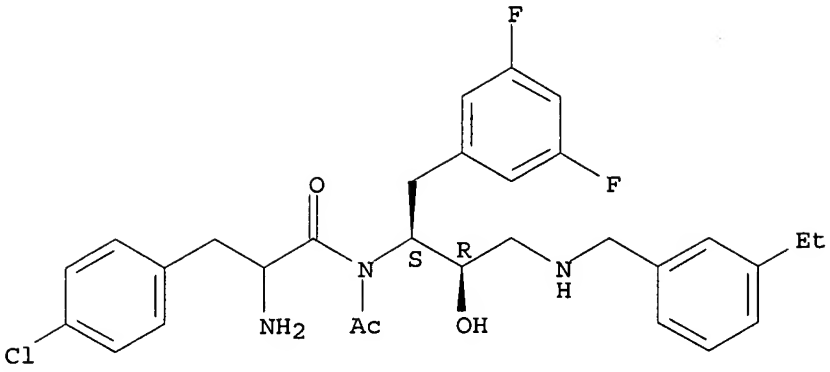
L2 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 488845-95-0 REGISTRY
ED Entered STN: 12 Feb 2003
CN Benzenepropanamide, N-acetyl-α-amino-4-chloro-N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H34 Cl F2 N3 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.18	3

Absolute stereochemistry.



Predicted Properties (PPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	1.43	pH 1 25 deg C	(1)
Bioconc. Factor (BCF)	1.44	pH 2 25 deg C	(1)
Bioconc. Factor (BCF)	1.44	pH 3 25 deg C	(1)
Bioconc. Factor (BCF)	1.47	pH 4 25 deg C	(1)
Bioconc. Factor (BCF)	2.05	pH 5 25 deg C	(1)
Bioconc. Factor (BCF)	29.39	pH 6 25 deg C	(1)
Bioconc. Factor (BCF)	890.74	pH 7 25 deg C	(1)
Bioconc. Factor (BCF)	7416.47	pH 8 25 deg C	(1)
Bioconc. Factor (BCF)	15851.29	pH 9 25 deg C	(1)
Bioconc. Factor (BCF)	17794.10	pH 10 25 deg C	(1)
Boiling Point (BP)	708.6+/-60.0 deg C	760 Torr	(1)
Density (DEN)	1.263+/-0.06 g/cm**3	760 Torr	(1)
Enthalpy of Vap. (HVAP)	108.81+/-3.0 kJ/mol	760 Torr	(1)
Flash Point (FP)	382.3+/-32.9 deg C		(1)
Freely Rotatable Bonds (FRB)	14		(1)
H acceptors (HAC)	6		(1)
H donors (HD)	4		(1)
Hydrogen Donors/Acceptors Sum (HDAS)	10		(1)
Koc (KOC)	3.08	pH 1 25 deg C	(1)
Koc (KOC)	3.08	pH 2 25 deg C	(1)
Koc (KOC)	3.09	pH 3 25 deg C	(1)
Koc (KOC)	3.16	pH 4 25 deg C	(1)
Koc (KOC)	4.40	pH 5 25 deg C	(1)
Koc (KOC)	63.07	pH 6 25 deg C	(1)
Koc (KOC)	1911.58	pH 7 25 deg C	(1)
Koc (KOC)	15916.13	pH 8 25 deg C	(1)
Koc (KOC)	34017.70	pH 9 25 deg C	(1)
Koc (KOC)	38187.07	pH 10 25 deg C	(1)
logD (LOGD)	1.80	pH 1 25 deg C	(1)
logD (LOGD)	1.80	pH 2 25 deg C	(1)
logD (LOGD)	1.80	pH 3 25 deg C	(1)
logD (LOGD)	1.81	pH 4 25 deg C	(1)
logD (LOGD)	1.96	pH 5 25 deg C	(1)
logD (LOGD)	3.11	pH 6 25 deg C	(1)
logD (LOGD)	4.60	pH 7 25 deg C	(1)

logD (LOGD)	5.52	pH 8 25 deg C	(1)
logD (LOGD)	5.85	pH 9 25 deg C	(1)
logD (LOGD)	5.90	pH 10 25 deg C	(1)
logP (LOGP)	5.904+/-0.820	25 deg C	(1)
Mass Intrinsic Solubility (ISLB.MASS)	0.00015 g/L	25 deg C	(1)
Mass Solubility (SLB.MASS)	1.9 g/L	pH 1 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.9 g/L	pH 2 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.9 g/L	pH 3 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.8 g/L	pH 4 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.3 g/L	pH 5 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.095 g/L	pH 6 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0031 g/L	pH 7 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00037 g/L	pH 8 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00017 g/L	pH 9 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00016 g/L	pH 10 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00051 g/L	Unbuffered Water pH 7.79 25 deg C	(1)
Molar Intrinsic Solubility (ISLB.MOL)	0.00000027 mol/L	25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0034 mol/L	pH 1 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0034 mol/L	pH 2 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0034 mol/L	pH 3 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0033 mol/L	pH 4 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0024 mol/L	pH 5 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00017 mol/L	pH 6 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000055 mol/L	pH 7 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000066 mol/L	pH 8 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000031 mol/L	pH 9 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000028 mol/L	pH 10 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000091 mol/L	Unbuffered Water pH 7.79 25 deg C	(1)
Molar Volume (MVOL)	441.5+/-3.0 cm**3/mol	20 deg C 760 Torr	(1)
Molecular Weight (MW)	558.06		(1)
pKa (PKA)	13.56+/-0.20	Most Acidic 25 deg C	(1)
pKa (PKA)	8.13+/-0.30	Most Basic 25 deg C	(1)
Polar Surface Area (PSA)	95.66 A**2		(1)
Vapor Pressure (VP)	4.52E-21 Torr	25 deg C	(1)

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.19 ((C) 1994-2006 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 138:136938 CA
TITLE: Preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease
INVENTOR(S): Gailunas, Andrea; Hom, Roy; John, Varghese; Maillard, Michel; Chrusciel, Robert Alan; Fisher, Jed; Jacobs, Jon; Freskos, John N.; Brown, David L.; Fobian, Yvette M.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07C233-35
SECONDARY: A61K031-164; A61P025-28
CLASSIFICATION: 23-18 (Aliphatic Compounds)
Section cross-reference(s): 1, 25, 27, 28
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006423	A1	20030123	WO 2002-US22255	20020711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2003109559	A1	20030612	US 2002-193044	20020711
EP 1409450	A1	20040421	EP 2002-750011	20020711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, IS, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504737	T2	20050217	JP 2003-512195	20020711
BR 2002011119	A	20051213	BR 2002-11119	20020711
NO 2004000139	A	20040226	NO 2004-139	20040112
ZA 2004000243	A	20041027	ZA 2004-243	20040113
PRIORITY APPLN. INFO.:			US 2001-304525P	20010711
			US 2001-308756P	20010730
			US 2001-341341P	20011217
			US 2001-341416P	20011217
			US 2001-344872P	20011221
			US 2001-380574P	20011221
			WO 2002-US22255	20020711

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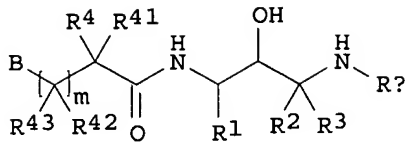

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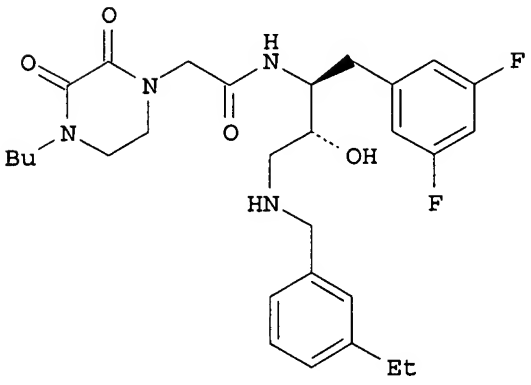

II

ABSTRACT:
The title compds. [I; m = 0-5; B = (un)substituted (hetero)aryl, (hetero)cycloalkyl; R4, R41 = H, CN, OCF3, etc.; R4 and R41 together = O; R42, R43 = H, CN, OCF3, etc.; R42 and R43 together = O; R1 = (CH2)1-2 S(O)0-2alkyl, substituted alkyl, aryl, etc.; R2 = H, alkyl, alkenyl, etc.; R3 = H, alkenyl, alkynyl, etc.; R2 and R3 taken together with the carbon atom to which they are attached form 3-7 membered carbocycle where one atom is optionally a heteroatom; Rc = H, alkyl, alkenyl, etc.], useful in treating Alzheimer's disease and other similar diseases characterized by deposition of A beta peptide in a mammal, were prepared E.g., a multi-step synthesis of (1S,2R)-II.HCl, starting from N-butylethylenediamine and di-Et oxalate, was given. The compds. I showed IC50 of < 50 μM against β-secretase. The compds. I are useful in pharmaceutical compns. and methods of treatment to reduce A beta peptide formation.

SUPPL. TERM: alkanamide aminohydroxypropyl prepn beta secretase inhibitor Alzheimer's disease; amyloid beta alkanamide aminohydroxypropyl prepn

INDEX TERM: Alzheimer's disease
(Lewy-body variant, treatment of; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Brain, disease
(amyloid angiopathy; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Brain, disease
(amyloidosis, hereditary cerebral hemorrhage type, Dutch type, treatment of; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Mental and behavioral disorders
(dementia, treatment of degenerative dementias; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Amyloidosis
(hereditary, cerebral hemorrhage type, Dutch type,

treatment of; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Anti-Alzheimer's agents
Cognition enhancers
Human
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Cognitive disorders
(treatment of mild cognitive impairment; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Alzheimer's disease
Down's syndrome
(treatment of; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: Amyloid
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: 158736-49-3, β-Secretase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM:

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488846-68-0P 488846-69-1P 488846-91-9P 488846-92-0P
488846-93-1P 488846-94-2P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: 488846-95-3P 488846-96-4P 488846-97-5P 488846-98-6P
488846-99-7P 488847-00-3P 488847-01-4P 488847-02-5P
488847-03-6P 488847-04-7P 488847-05-8P 488847-06-9P
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ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: 96-32-2, Methyl bromoacetate 105-53-3, Diethyl malonate 542-69-8, 1-Iodobutane 930-68-7, Cyclohex-2-enone 4530-20-5, tert-Butoxycarbonyl-glycine 4926-28-7, 2-Bromo-4-methylpyridine 5292-43-3, tert-Butyl bromoacetate 5625-67-2, Oxopiperazine 19522-69-1, N-Butylethylenediamine 33777-32-1, 6-Propylcyclohex-2-en-1-one 59702-31-7, N-Ethylpiperazin-2,3-dione 99208-98-7, Methyl (S)-2-(trifluoromethylsulfonyloxy)propionate 138397-85-0 488846-89-5 488846-90-8

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: 2385-28-6P 22274-75-5P 39762-51-1P 59702-09-9P 76003-29-7P 488846-70-4P 488846-71-5P 488846-72-6P 488846-73-7P 488846-74-8P 488846-75-9P 488846-76-0P 488846-77-1P 488846-78-2P 488846-79-3P 488846-80-6P 488846-81-7P 488846-82-8P 488846-83-9P 488846-84-0P 488846-85-1P 488846-86-2P 488846-87-3P 488846-88-4P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

INDEX TERM: 150234-52-9 186142-26-7 186142-28-9 252256-37-4 288584-07-6 288584-08-7 478686-67-8 491669-24-0

ROLE: PRP (Properties)
(unclaimed sequence; preparation of N-(3-amino-2-hydroxy-propyl) substituted alkanamides as inhibitors of the beta secretase enzyme for treating Alzheimer's disease)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Kissei Pharmaceutical; EP 0200406 A 1986 CAPLUS
(2) Marlowe, C; US 6211183 B1 2001 CAPLUS
(3) Squibb & Sons Inc; GB 2184730 A 1987 CAPLUS
(4) Squibb & Sons Inc; EP 0580402 A 1994 CAPLUS
(5) Upjohn Co; WO 0202512 A 2002 CAPLUS

L2 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 181289-50-9 REGISTRY
ED Entered STN: 26 Sep 1996
CN Benzenepropanol, β-[bis(phenylmethyl)amino]-α-[[(2-methylpropyl)amino]methyl]-, (αR,βS)-, monoacetate (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanol, β-[bis(phenylmethyl)amino]-α-[[(2-methylpropyl)amino]methyl]-, [R-(R*,S*)]-, monoacetate (salt)
FS STEREOSEARCH
MF C28 H36 N2 O . C2 H4 O2
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Ring System Data

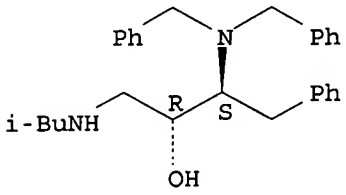
Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count

C6	C6	6	C6	46.150.18	3 in CM 1

CM 1

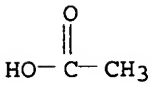
CRN 169331-42-4
CMF C28 H36 N2 O

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2



18 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 134:86548 CA
TITLE: Preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; De Crescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Deyadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 85 pp., Cont.-in-part of U. S. Ser. No. 402,419, abandoned
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-4025
SECONDARY: C07D405-12
US PATENT CLASSIF.: 514422000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6172101	B1	20010109	US 1998-894984	19980423	
WO 9628465	A1	19960919	WO 1996-US2683	19960307	

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

PRIORITY APPLN. INFO.:

US 1995-402419	19950310
WO 1996-US2683	19960307
US 1995-474117	19950607

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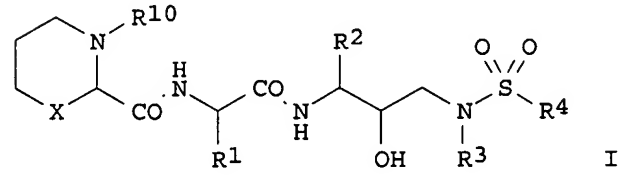

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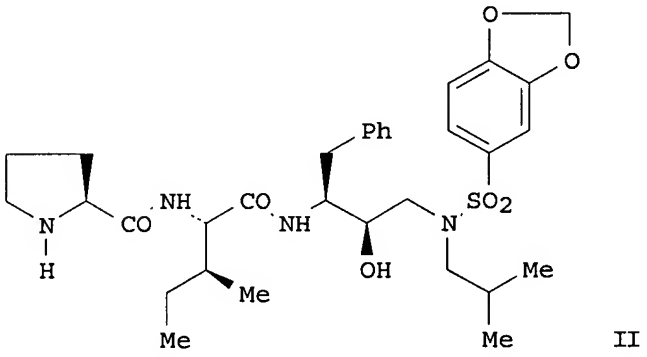

II

ABSTRACT:
Heterocyclylcarbonyl amino acids, such as I [R1 = alkyl, alkenyl, alkynyl, etc.; R2 = alkyl, arylalkyl, alkylthioalkyl, arylthioalkyl, etc.; R3 = alkyl, cycloalkyl; R4 = aryl, heteroaryl; R10 = H, alkyl, nitrogen protecting group, etc., X = CH2, bond], were prepared for pharmaceutical use as HIV protease inhibitors for inhibiting retroviral proteases, such as human immunodeficiency virus (HIV) protease, prophylactically preventing retroviral infection or the spread of a retrovirus, and treatment of a retroviral infection. Thus, II was prepared by a multistep synthetic sequence starting from N-protected-L-phenylalanine, -L-isoleucine, -L-proline, isobutylamine, and 1,3-benzodioxole. The prepared heterocyclylcarbonyl amino acids were tested via an HIV inhibition assay.

SUPPL. TERM: heterocyclylcarbonyl amino acid prepn HIV protease inhibitor

INDEX TERM: Anti-AIDS agents
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 144114-21-6, Retropepsin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HIV; preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease

inhibitors)

INDEX TERM: 42807-45-4P 111060-52-7P 111060-64-1P 127927-43-9P
143224-62-8P 149451-80-9P 149451-81-0P 157445-95-9P
158380-73-5P 158380-76-8P 160232-08-6P 169280-56-2P
169280-63-1P 169280-71-1P 169331-42-4P 170359-14-5P
170359-16-7P 174303-68-5P 174391-93-6P 181124-41-4P
181124-46-9P 183005-02-9P 183005-03-0P 183005-04-1P

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 157566-75-1P 159005-71-7P 159006-11-8P 159006-14-1P
159006-17-4P 169280-61-9P 169280-62-0P 169280-66-4P
169280-67-5P 174303-70-9P 181124-38-9P 181289-50-9P
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183581-22-8P 183581-50-2P 183813-28-7P

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions
74-97-5, Bromochloromethane 78-81-9, Isobutylamine
98-09-9, Benzenesulfonyl chloride 98-59-9,
4-Methylbenzenesulfonyl chloride 98-68-0,
4-Methoxybenzenesulfonyl chloride 98-74-8,
4-Nitrobenzenesulfonyl chloride 100-39-0, Benzyl bromide
100-52-7, Benzaldehyde, reactions 121-51-7,
3-Nitrobenzenesulfonyl chloride 274-09-9, 1,3-Benzodioxole
333-20-0, Potassium thiocyanate 496-16-2,
2,3-Dihydrobenzofuran 593-71-5, Chloroiodomethane
1148-11-4, N-(Benzyloxycarbonyl)-L-proline 1149-26-4,
N-(Benzyloxycarbonyl)-L-valine 1762-95-4, Ammonium
thiocyanate 3182-95-4, L-Phenylalaninol 3391-99-9
3392-08-3 7790-94-5, Chlorosulfonic acid 10605-21-7
13139-16-7, N-(tert-Butyloxycarbonyl)-L-isoleucine
20887-95-0, N-(tert-Butyloxycarbonyl)-L-cysteine
26049-94-5 62965-10-0 63039-48-5 63758-12-3
75315-63-8, N-(Benzyloxycarbonyl)succinimide 112898-23-4
116661-86-0

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 1718-39-4P 18101-58-1P 79213-74-4P 111138-83-1P
115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride
115010-11-2P 128018-43-9P 128018-44-0P 145708-16-3P,
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6-Benzothiazolesulfonyl chloride 183004-94-6P
183004-95-7P 183004-96-8P 183553-79-9P 183553-80-2P
183553-83-5P 183553-90-4P 183553-91-5P 183553-95-9P
183553-99-3P 183554-00-9P 183554-01-0P 183554-08-7P
183554-27-0P 183556-67-4P 183556-74-3P 183581-49-9P
183581-52-4P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 127943-39-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

(1) Anon; DE 0104041 1984
(2) Anon; EP 0114993 A2 1984 CAPLUS
(3) Anon; WO 8403044 1984 CAPLUS
(4) Anon; EP 0172347 A2 1986 CAPLUS
(5) Anon; EP 0223437 A2 1987 CAPLUS
(6) Anon; GB 2184730 1987 CAPLUS
(7) Anon; EP 0264795 A2 1988 CAPLUS
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(62) Ryono; US 4616088 1986 CAPLUS
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REFERENCE 2

ACCESSION NUMBER: 134:71903 CA
TITLE: Preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 401,838, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-18
SECONDARY: A61K031-343; A61K031-4192; C07C311-17; C07C249-18; C07C307-79
US PATENT CLASSIF.: 514228200
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6169085	B1	20010102	US 1999-411374	19991004
US 6380188	B1	20020430	US 2000-672449	20000929
US 2003191166	A1	20031009	US 2002-82123	20020226
US 6667307	B2	20031223		
US 2004147758	A1	20040729	US 2003-677729	20031003
US 7045518	B2	20060516		
PRIORITY APPLN. INFO.:			US 1995-401838	19950310
			WO 1996-US2682	19960307
			US 1997-913069	19971219
			US 1999-411374	19991004
			US 2000-672449	20000929
			US 2002-82123	20020226

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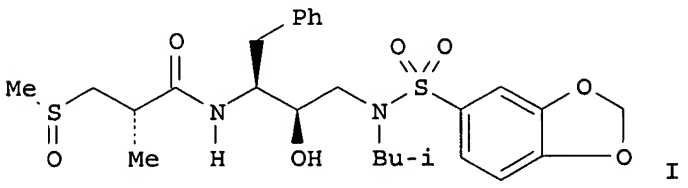

I

ABSTRACT:
Sulfonylalkanoylamino hydroxyethylamino sulfonamide compds.
R5S(O)t(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2SOMe, CH2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = benzo-fused heteroaryl or heterocyclyl; R5 = alkyl, alkenyl, alkynyl, aryl; t = 0-2) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-(methylsulfonyl)propanamide was prepared and assayed for HIV protease inhibitory activity (IC50 = 2 nM; EC50 = 20 nM). The corresponding methylsulfinyl derivative I (claimed compound) showed IC50 values 2 and 7 nM and EC50
values 52 and 80 nM for the two isomers.

SUPPL. TERM: sulfonylalkanoylamino hydroxyethylamino sulfonamide prepn
protease inhibitor; benzodioxolesulfonamide
sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzofuransulfonamide
sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzothiazolesulfonamide
sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzodioxanesulfonamide
sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor

INDEX TERM: Anti-AIDS agents
Antiviral agents
Human immunodeficiency virus 1
Retroviridae
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Peptides, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 123054-12-6P 127927-43-9P 127943-39-9P 149451-81-0P
157445-95-9P 157566-75-1P 157566-76-2P 157566-81-9P
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159005-71-7P 160232-08-6P 169280-56-2P 169280-62-0P
169280-63-1P 169280-66-4P 169280-71-1P 169331-41-3P
170359-16-7P 174303-66-3P 181124-38-9P 181124-46-9P
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ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 9001-92-7, Protease 144114-21-6, Retropepsin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1 63-91-2, L-Phenylalanine, reactions 74-97-5

78-81-9 96-33-3 98-74-8 100-52-7, Benzaldehyde, reactions 107-10-8, 1-Propanamine, reactions 107-85-7 109-73-9, 1-Butanamine, reactions 121-51-7 274-09-9, 1,3-Benzodioxole 333-20-0 593-71-5 3182-95-4 4224-69-5 4410-99-5, Benzeneethanethiol 10605-21-7 20609-71-6 23095-31-0 26049-94-5 63758-12-3 74431-52-0 76497-39-7 81000-54-6 116661-86-0 143224-62-8 181124-54-9 201683-41-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 496-16-2P 1718-39-4P 18101-58-1P 36525-60-7P 42807-45-4P 79213-74-4P 81026-69-9P 111060-52-7P 111060-64-1P 111060-81-2P 111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 128018-43-9P 128018-44-0P 143224-81-1P 143224-92-4P 143224-94-6P 143224-99-1P 143225-00-7P 143225-04-1P 143291-14-9P 145708-16-3P, 6-Benzothiazolesulfonic acid 149451-80-9P 157566-88-6P 157566-94-4P 157566-99-9P 157567-00-5P 157567-01-6P 157567-02-7P 157567-03-8P 157567-07-2P 157567-08-3P 157567-09-4P 158380-73-5P 158380-76-8P 159005-59-1P 169280-61-9P 169280-67-5P 169280-89-1P 169280-90-4P 169280-91-5P 169331-42-4P 174303-68-5P 174391-93-6P 174796-83-9P 181124-40-3P, 6-Benzothiazolesulfonyl chloride 181124-41-4P 183004-94-6P 183004-95-7P 183004-96-8P 183004-97-9P 183004-99-1P 183005-01-8P 183005-04-1P 183182-30-1P 183554-21-4P 201682-28-2P 201683-24-1P 201683-42-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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(2) Anon; EP 0114993 1984 CAPLUS
(3) Anon; WO 8403044 1984 CAPLUS
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(20) Anon; WO 9404493 1994 CAPLUS
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(24) Anon; WO 9533464 1995 CAPLUS
(25) Anon; WO 9602682 1996 CAPLUS
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(58) Ryono; US 4616088 1986 CAPLUS
(59) Silcox; J Heterocycl Chem 1967, V4, P166

REFERENCE 3

ACCESSION NUMBER: 133:350519 CA
TITLE: Synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan Raj; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 148 pp., Cont.-in-part of U.S. Ser. No. 402,450, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07C311-16
SECONDARY: A61K031-18
US PATENT CLASSIF.: 564092000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 28
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6150556	A	20001121	US 1995-479071	19950607
CA 2215025	AA	19960919	CA 1996-2215025	19960307
WO 9628464	A1	19960919	WO 1996-US2685	19960307

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
AU 9653561	A1	19961002	AU 1996-53561	19960307	
AU 704360	B2	19990422			
BR 9607543	A	19971223	BR 1996-7543	19960307	
EP 813543	A1	19971229	EP 1996-910337	19960307	
EP 813543	B1	20050914			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
CN 1196732	A	19981021	CN 1996-193618	19960307	
JP 11501921	T2	19990216	JP 1996-527649	19960307	
EP 1076062	A1	20010214	EP 2000-114911	19960307	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
EP 1188766	A1	20020320	EP 2001-129219	19960307	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
PL 185108	B1	20030228	PL 1996-322163	19960307	
PL 185543	B1	20030530	PL 1996-352508	19960307	
EE 4376	B1	20041015	EE 1997-200	19960307	
CZ 294966	B6	20050413	CZ 1997-2825	19960307	
AT 304550	E	20050915	AT 1996-910337	19960307	
ES 2249779	T3	20060401	ES 1996-910337	19960307	
NO 9704149	A	19971105	NO 1997-4149	19970909	
US 6316496	B1	20011113	US 2000-495334	20000201	
US 6388132	B1	20020514	US 2000-694783	20001024	
US 2003204097	A1	20031030	US 2002-97642	20020315	
US 6683210	B2	20040127			
US 6861539	B1	20050301	US 2003-638479	20030812	
US 2005227926	A1	20051013	US 2005-36606	20050118	
PRIORITY APPLN. INFO.:			US 1995-402450	19950310	
			US 1995-479071	19950607	
			EP 1996-910337	19960307	
			WO 1996-US2685	19960307	
			US 1998-913096	19980121	
			US 2000-495334	20000201	
			US 2000-694783	20001024	
			US 2002-97642	20020315	
			US 2003-638479	20030812	

ABSTRACT:
Peptides R13NHCH2CONHCHR1CONHCH(CH2Ph)CH(OH)CH2N(Bu-i)SO2R4 (R1 = C1-5alkyl, C2-5alkynyl; R4 = aryl; R13 = aralkyl, cycloalkyl, alkoxyalkyl), including stereoisomers, pharmaceutically acceptable salts, and prodrugs, were prepared as retroviral protease inhibitors. Thus, compound 2S-[[(methylamino)acetyl]amino]-N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-3,3-dimethylbutanamide was prepared and shown to be an effective HIV protease inhibitor (IC50 = 2 nM, EC50 = 18 nM).

SUPPL. TERM: amino acid hydroxyethylamino sulfonamide prepn protease inhibitor; heterocyclyl sulfonyl chloride intermediate protease inhibitor

INDEX TERM: Sulfonyl halides
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chlorides; synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Human immunodeficiency virus
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Amino acids, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 181124-41-4P 183004-93-5P 183005-03-0P 183556-68-5P 183556-69-6P 183556-70-9P 183556-71-0P 183556-72-1P 183556-76-5P 183556-77-6P 183556-78-7P 183556-79-8P 183556-87-8P 183556-88-9P 183556-89-0P 183556-90-3P 183556-92-5P 183556-94-7P 183556-95-8P 183556-96-9P 183556-98-1P 183556-99-2P 183557-00-8P 183812-71-7P 303758-70-5P 303759-58-2P 303759-61-7P 303759-63-9P 303759-65-1P

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions 74-89-5, Methylamine, reactions 74-97-5, Bromochloromethane 78-81-9, Isobutylamine 79-11-8, Chloroacetic acid, reactions 98-74-8, 4-Nitrobenzenesulfonyl chloride 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 109-85-3, 2-Methoxyethylamine 141-43-5, 2-Hydroxyethylamine, reactions 274-09-9, 1,3-Benzodioxole 541-88-8, Chloroacetic anhydride 593-71-5, Chloroiodomethane 765-30-0, Cyclopropylamine 1762-95-4, Ammonium thiocyanate 3182-95-4, L-Phenylalaninol 10605-21-7 22118-09-8, Bromoacetyl chloride 26049-94-5 63758-12-3, 1,4-Benzodioxan-6-sulfonyl chloride 112898-23-4 116661-86-0 128018-43-9 159005-61-5 159005-71-7 159006-16-3 159006-17-4 169280-91-5 181124-54-9 183556-80-1

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 496-16-2P, 2,3-Dihydrobenzofuran 1718-39-4P 18101-58-1P 42807-45-4P 79213-74-4P 111060-52-7P 111060-64-1P 111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 127927-43-9P 127943-39-9P 128018-44-0P 143224-62-8P 145708-16-3P, 6-Benzothiazolesulfonic acid 149451-80-9P 149451-81-0P 157566-75-1P 158380-73-5P 158380-76-8P 159005-59-1P 159006-10-7P 159006-11-8P 159006-12-9P 159006-18-5P 160232-08-6P 169280-56-2P 169280-61-9P 169280-62-0P 169280-66-4P 169280-67-5P 169280-71-1P 169280-90-4P 169331-41-3P 169331-42-4P 170359-16-7P 174303-68-5P 174303-69-6P 174303-70-9P 174303-71-0P 174391-93-6P 181124-40-3P, 6-Benzothiazolesulfonyl chloride 181124-46-9P 181289-50-9P 181289-51-0P 181289-52-1P 181289-53-2P 181289-54-3P 183004-94-6P 183004-95-7P 183004-96-8P 183004-97-9P 183005-02-9P 183005-04-1P 183553-48-2P 183553-49-3P 183553-79-9P 183553-80-2P 183553-81-3P 183553-83-5P 183553-84-6P 183553-85-7P 183553-90-4P 183553-91-5P 183553-92-6P 183553-93-7P 183553-95-9P 183553-96-0P 183553-97-1P 183553-99-3P 183554-00-9P 183554-02-1P 183554-08-7P 183554-09-8P 183554-10-1P 183554-27-0P 183554-30-5P 183554-33-8P 183556-67-4P 183556-73-2P 183556-74-3P 183556-75-4P 183556-81-2P 183556-82-3P 183556-83-4P 183556-84-5P 183556-91-4P 183556-93-6P 183556-97-0P 183812-73-9P 201682-28-2P 201682-92-0P 303759-39-9P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino

sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

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(2) Anon; EP 0114993 1984 CAPLUS
(3) Anon; WO 8403044 1984 CAPLUS
(4) Anon; EP 0172347 1986 CAPLUS
(5) Anon; EP 0223437 1987 CAPLUS
(6) Anon; GB 2184730 1987 CAPLUS
(7) Anon; EP 0264795 1988 CAPLUS
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(10) Anon; EP 0342541 1989 CAPLUS
(11) Anon; EP 0346847 1989 CAPLUS
(12) Anon; GB 2209752 1989 CAPLUS
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(16) Anon; EP 0393457 1990 CAPLUS
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(18) Anon; EP 0468641 1992 CAPLUS
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(59) Tung; US 5585397 1996 CAPLUS

(60) Vazquez; US 5744481 1998 CAPLUS

REFERENCE 4

ACCESSION NUMBER: 133:335463 CA
TITLE: Synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Belekudru; Nagarajan, Srinivasan Raj; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 148 pp., Cont.-in-part of U.S. Ser. No. 402,450, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-18
SECONDARY: C07C311-17
US PATENT CLASSIF.: 514604000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 28
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6143788	A	20001107	US 1998-913096	19980121
WO 9628464	A1	19960919	WO 1996-US2685	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
EP 1188766	A1	20020320	EP 2001-129219	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
US 6388132	B1	20020514	US 2000-694783	20001024
US 2003204097	A1	20031030	US 2002-97642	20020315
US 6683210	B2	20040127		
US 6861539	B1	20050301	US 2003-638479	20030812
US 2005227926	A1	20051013	US 2005-36606	20050118

PRIORITY APPLN. INFO.:

US 1995-402450	19950310
WO 1996-US2685	19960307
US 1995-479071	19950607
EP 1996-910337	19960307
US 1998-913096	19980121
US 2000-495334	20000201
US 2000-694783	20001024
US 2002-97642	20020315
US 2003-638479	20030812

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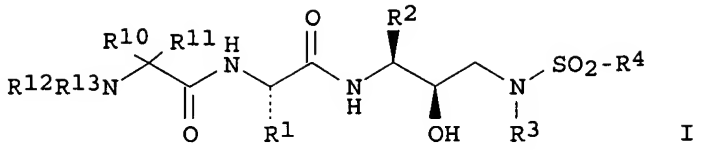

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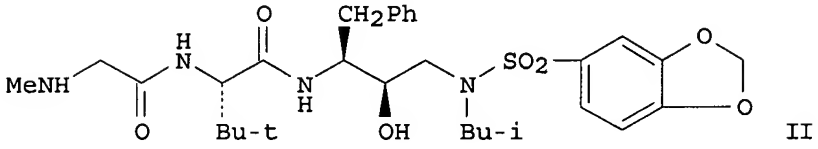

II

ABSTRACT:
Peptides I [R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2S(O)Me, CH2SO2Me, CMe2SMe, CMe2S(O)Me, CMe2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl or benzo-fused 5-6 membered heteroaryl or heterocyclyl; R10 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R11 = any group given for R10 or benzyl, imidazolylmethyl, CH2CH2CONH2, CH2CONH2, CH2CH2SMe, CH2SMe or sulfone or sulfoxide derivs.; R12, R13 = H, alkyl, aralkyl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, aryl or heteroaryl, where cycloalkyl or heteroaryl may be benzo fused (with provisos)] were prepared as retroviral protease inhibitors. Thus, compound II was prepared and shown to be an effective HIV protease inhibitor (IC50 = 2 nM, EC50 = 18 nM).

SUPPL. TERM: amino acid hydroxyethylamino sulfonamide prepn protease inhibitor; heterocyclyl sulfonyl chloride intermediate protease inhibitor

INDEX TERM: Sulfonyl halides
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chlorides; synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Human immunodeficiency virus
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

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183556-72-1P 183556-77-6P 183556-79-8P 183556-87-8P
183556-88-9P 183556-92-5P 183556-94-7P 183556-98-1P
183556-99-2P 183557-00-8P 183812-73-9P 303759-58-2P
303759-61-7P 303759-63-9P 303759-65-1P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bis-amino acid hydroxyethylamino

sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions 74-89-5, Methylamine, reactions 74-97-5, Bromochloromethane 78-81-9, Isobutylamine 79-11-8, Chloroacetic acid, reactions 98-95-3, Nitrobenzene, reactions 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 109-85-3, 2-Methoxyethylamine 141-43-5, reactions 274-09-9, 1,3-Benzodioxole 496-16-2, 2,3-Dihydrobenzofuran 541-88-8, Chloroacetic anhydride 593-71-5, Chloroiodomethane 765-30-0, Cyclopropylamine 1762-95-4 3182-95-4, L-Phenylalaninol 10605-21-7 22118-09-8, Bromoacetyl chloride 26049-94-5 63758-12-3, 1,4-Benzodioxan-6-sulfonyl chloride 112898-23-4 116661-86-0 157446-10-1 159005-61-5 159005-71-7 181124-54-9

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 1718-39-4P, n-(4-Sulfonamidophenyl)thiourea 18101-58-1P 42807-45-4P 79213-74-4P 111060-52-7P 111060-64-1P 111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 127927-43-9P 127943-39-9P 128018-43-9P 128018-44-0P 143224-62-8P 145708-16-3P, 6-Benzothiazolesulfonic acid 149451-80-9P 149451-81-0P 157566-75-1P 158380-73-5P 158380-76-8P 159005-59-1P 159006-10-7P 159006-11-8P 159006-12-9P 159006-16-3P 159006-17-4P 159006-18-5P 160232-08-6P 169280-56-2P 169280-61-9P 169280-62-0P 169280-66-4P 169280-67-5P 169280-71-1P 169280-90-4P 169280-91-5P 169331-41-3P 169331-42-4P 170359-16-7P 174303-68-5P 174303-69-6P 174303-70-9P 174303-71-0P 174391-93-6P 181124-40-3P, 6-Benzothiazolesulfonyl chloride 181124-41-4P 181124-46-9P 181289-50-9P 181289-51-0P 181289-52-1P 181289-53-2P 181289-54-3P 183004-93-5P 183004-94-6P 183004-95-7P 183004-96-8P 183004-97-9P 183005-02-9P 183005-03-0P 183005-04-1P 183553-48-2P 183553-49-3P 183553-79-9P 183553-80-2P 183553-81-3P 183553-83-5P 183553-84-6P 183553-85-7P 183553-90-4P 183553-91-5P 183553-92-6P 183553-93-7P 183553-95-9P 183553-96-0P 183553-97-1P 183553-99-3P 183554-00-9P 183554-01-0P 183554-02-1P 183554-08-7P 183554-09-8P 183554-10-1P 183554-21-4P 183554-30-5P 183554-33-8P 183556-67-4P 183556-73-2P 183556-74-3P 183556-75-4P 183556-76-5P 183556-78-7P 183556-81-2P 183556-82-3P 183556-83-4P 183556-84-5P 183556-89-0P 183556-90-3P 183556-93-6P 183556-95-8P 183556-96-9P 183812-71-7P 183812-74-0P 201682-28-2P 201682-92-0P 251113-93-6P 303758-41-0P 303758-70-5P 303759-39-9P 303759-41-3P 303759-44-6P 303765-21-1P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bis-amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

(1) Anon; EP 0114993 1984 CAPLUS
(2) Anon; EP 0172347 1986 CAPLUS
(3) Anon; EP 0233437 1987 CAPLUS
(4) Anon; EP 0337714 1989 CAPLUS
(5) Anon; EP 0356223 1990 CAPLUS
(6) Anon; EP 0389898 1990 CAPLUS
(7) Anon; EP 0393445 1990 CAPLUS
(8) Anon; EP 0393457 1990 CAPLUS
(9) Anon; EP 0402646 1990 CAPLUS

(10) Anon; EP 0468641 1992 CAPLUS
(11) Anon; WO 9208699 1992 CAPLUS
(12) Anon; WO 9313066 1993 CAPLUS
(13) Anon; WO 9404492 1994 CAPLUS
(14) Anon; WO 9404493 1994 CAPLUS
(15) Anon; WO 9405639 1994 CAPLUS
(16) Anon; WO 9410134 1994 CAPLUS
(17) Anon; WO 9506030 1995 CAPLUS
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(35) Tung; US 5585397 1996 CAPLUS
(36) Vazquez; US 5744481 1998 CAPLUS

REFERENCE 5

ACCESSION NUMBER: 133:322130 CA
TITLE: Synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors
INVENTOR(S): Kunda, Sastry A.; Letendre, Leo J.; De Crescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 95 pp., Cont.-in-part of U.S. 5,756,533.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D277-62
SECONDARY: C07D207-18; C07D319-16; C07D307-79
US PATENT CLASSIF.: 548197000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 28
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6140505	A	20001031	US 1998-80928	19980519
US 5756533	A	19980526	US 1995-474052	19950607
EP 1258491	A1	20021120	EP 2002-11526	19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
WO 9959989	A1	19991125	WO 1999-US7047	19990518
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,				

TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9938604	A1	19991206	AU 1999-38604	19990518
US 6310080	B1	20011030	US 1999-451920	19991201
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		
US 2003216435	A1	20031120	US 2002-200589	20020723
US 6730669	B2	20040504		
US 2004260095	A1	20041223	US 2004-760125	20040120

PRIORITY APPLN. INFO.:

US 1995-402287 19950310
US 1995-474052 19950607
US 1995-391873 19950222
EP 1996-907135 19960307
US 1998-80928 19980519
WO 1999-US7047 19990518
US 1999-451920 19991201
US 2001-836443 20010418
US 2002-200589 20020723

ABSTRACT:
Benzo-fused heterocyclic sulfonyl halides for the preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors were obtained by a process comprising reacting a benzo-fused heterocyclic compound with an SO3 complex in the presence of a water immiscible, non-reactive solvent at 0-75°, cooling, if necessary, to a temperature of from about -25° to about 65° and then adding oxalyl halide. Thus, N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-2S-[(pyrrolidin-1-yl)acetylamino]-3,3-dimethylbutanamide was prepared and shown to be an effective HIV protease inhibitor (IC50 = 3 nM, EC50 = 7 nM).

SUPPL. TERM: amino acid hydroxyethylamine sulfonamide prepn protease inhibitor; heterocyclyl sulfonyl chloride intermediate protease inhibitor

INDEX TERM: Sulfonyl halides
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chlorides; synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: Human immunodeficiency virus
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: Amino acids, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 183812-50-2P 183812-51-3P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 174303-65-2P 183553-66-4P 183553-78-8P 183553-82-4P

183553-86-8P 183554-03-2P 183554-04-3P 183554-05-4P
183554-07-6P 183594-99-2P 183812-53-5P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 9001-92-7, Protease
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 127943-39-9P 201682-92-0P
ROLE: BYP (Byproduct); PREP (Preparation)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 169331-41-3P
ROLE: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions 74-97-5, Bromochloromethane 78-81-9, Isobutylamine 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-74-8, 4-Nitrobenzenesulfonyl chloride 100-52-7, Benzaldehyde, reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride 123-75-1, Pyrrolidine, reactions 274-09-9, 1,3-Benzodioxole 496-16-2, 2,3-Dihydrobenzofuran 541-88-8, Chloroacetic anhydride 593-71-5, Chloroiodomethane 1762-95-4 3182-95-4, L-Phenylalaninol 5292-43-3, tert-Butyl bromoacetate 6628-74-6, 1-Pyrrolidineacetic acid hydrochloride 10605-21-7 26049-94-5 62965-10-0 63039-48-5 63758-12-3, 1,4-Benzodioxan-6-sulfonyl chloride 112898-23-4 116661-86-0 157446-10-1 159005-61-5 181124-54-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

INDEX TERM: 1718-39-4P 18101-58-1P 37386-15-5P, 1-Pyrrolidineacetic acid 42807-45-4P 79213-74-4P 111060-52-7P 111060-64-1P 111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 127927-43-9P 128018-43-9P 128018-44-0P 143225-04-1P 145708-16-3P, 6-Benzothiazolesulfonic acid 149451-80-9P 149451-81-0P 157445-95-9P 157566-75-1P 157566-99-9P 158380-73-5P 158380-76-8P 159005-59-1P 159005-71-7P 159006-10-7P 159006-11-8P 159006-12-9P 159006-13-0P 159006-14-1P 159006-15-2P 159006-18-5P 160232-08-6P 169280-56-2P 169280-61-9P 169280-62-0P 169280-63-1P 169280-66-4P 169280-67-5P 169280-71-1P 169280-89-1P 169280-90-4P 169280-91-5P 169331-42-4P 170359-16-7P 174303-68-5P 174303-69-6P 174303-70-9P 174303-71-0P 174391-93-6P 181124-38-9P 181124-40-3P, 6-Benzothiazolesulfonyl chloride 181124-41-4P 181124-46-9P 181289-50-9P 181289-51-0P 181289-52-1P 181289-53-2P 181289-54-3P 183004-94-6P 183004-95-7P 183004-96-8P 183004-97-9P 183005-02-9P 183005-03-0P 183005-04-1P 183553-47-1P 183553-48-2P 183553-49-3P

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183556-73-2P 183556-74-3P 183556-75-4P 183556-83-4P
183556-84-5P 183812-52-4P 201682-28-2P 303112-81-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of benzo-fused heterocyclic sulfonyl chlorides for preparation of amino acid hydroxyethylamine sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Anon; WO 9907047
(2) Anon; EP 0254577 1988 CAPLUS
(3) Anon; EP 0583960 A2 1994 CAPLUS
(4) Anon; EP 0583960 1994 CAPLUS
(5) Anon; WO 9622287 1996 CAPLUS
(6) Anon; WO 9628418 1996 CAPLUS
(7) Anon; WO 9718205 1997 CAPLUS
(8) Getman; US 5756533 1998 CAPLUS
(9) Gorge, D; J Heterocyclic Chem 1989, V26, P1793
(10) Hartman; J Heterocyclic Chem 1989, V26, P1793 CAPLUS
(11) Hartman; J Med Chem 1992, V35, P3822 CAPLUS
(12) Miller; US 5387681 1995 CAPLUS
(13) Susan, B; The Merck Index, Eleventh Edition 1989, P598

REFERENCE 6

ACCESSION NUMBER: 132:6692 CA
TITLE: benzo fused heterocyclo sulfonyl halide intermediates for the preparation of amino acids as HIV protease inhibitors
INVENTOR(S): Kunda, Sastry A.; Letendre, Leo J.; De Crescenzo, Gary A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D317-62
SECONDARY: C07D319-18; C07D311-58; C07D339-06; C07D307-79
CLASSIFICATION: 67-3 (Catalysis, Reaction Kinetics, and Inorganic Reaction Mechanisms)
Section cross-reference(s): 1, 7, 28, 63
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959989	A1	19991125	WO 1999-US7047	19990518

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6140505	A	20001031	US 1998-80928	19980519
AU 9938604	A1	19991206	AU 1999-38604	19990518
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		
PRIORITY APPLN. INFO.:			US 1998-80928	19980519
			US 1995-402287	19950310
			US 1995-474052	19950607
			WO 1999-US7047	19990518
			US 1999-451920	19991201

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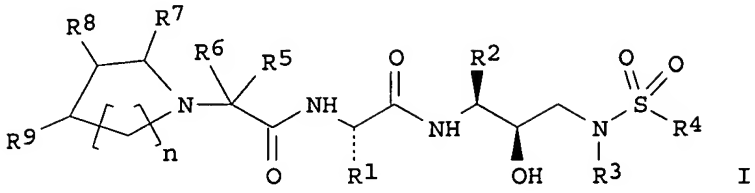

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ABSTRACT:
Sulfonyl amino acids I (R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, Ch2SOMe, Ch2SO2Me, CMe2SMe, CMeSOMe; R2 = alkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl; R3 = alkyl, cycloalkyl, cycloalkylalkyl; R4 = substituted heterocycle, R5 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R6 = H, alkyl, hydroxyalkyl, alkoxyalkyl, alkylamide, sulfone, alkylthioalkyl; R7-R9 = H, substituted heteroaryl, benzo) were prepared as HIV protease inhibitors. Process for preparing a benzo fused heterocyclo sulfonyl halide intermediate, comprising reacting a benzo fused heterocyclic compound with a -SO3- complex in the presence of a solvent and then adding oxalyl halide. Thus, amino acid I (R1 = CHMeEt, R2 = Bn, R3 = CH2CHMe3, R4 = Ph, R5-E9 = H, n = 1) was prepared and tested as HIV protease inhibitor (IC50 = 4 nM).

SUPPL. TERM: amino acid sulfonyl protease inhibitor prepn antiviral; benzo fused heterocyclo sulfonyl halide prepn synthon antiviral

INDEX TERM: Antiviral agents
Synthons
(benzo fused heterocyclo sulfonyl halide intermediates for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: Amino acids, preparation
Heterocyclic compounds
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzo fused heterocyclo sulfonyl halide intermediates for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: 157445-95-9P 169280-61-9P 169280-62-0P 174303-65-2P
174303-69-6P 181124-38-9P 181124-41-4P 181289-50-9P
181289-51-0P 181289-54-3P 183004-93-5P 183005-03-0P
183553-47-1P 183553-66-4P 183553-78-8P 183553-79-9P
183553-82-4P 183553-83-5P 183553-86-8P 183553-87-9P
183553-89-1P 183553-94-8P 183553-98-2P 183554-03-2P
183554-04-3P 183554-05-4P 183554-07-6P 183554-15-6P
183594-99-2P 183812-53-5P 251113-88-9P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(benzo fused heterocyclo sulfonyl halide intermediates
for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: 144114-21-6, Retropepsin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzo fused heterocyclo sulfonyl halide intermediates
for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions
74-97-5, Bromochloromethane 87-69-4, L-Tartaric acid, reactions 110-46-3, Isoamylnitrite 144-62-7, Ethanedioic acid, reactions 274-09-9, 1,3-Benzodioxole 333-20-0, Potassium thiocyanate 593-71-5, Chloroiodomethane
1762-95-4, Ammonium thiocyanate 3182-95-4,
L-Phenylalaninol 3392-08-3 5292-43-3,
tert-Butylbromoacetate 10605-21-7 13139-16-7
26049-94-5 62965-10-0 105181-72-4 111138-83-1
181124-40-3, 6-Benzothiazolesulfonyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(benzo fused heterocyclo sulfonyl halide intermediates
for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: 1718-39-4P 6628-74-6P 18101-58-1P 42807-45-4P
79213-74-4P 99113-35-6P 111060-52-7P 111060-64-1P
115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride
115010-11-2P 123054-12-6P 127927-43-9P 127943-39-9P
128018-44-0P 143224-62-8P 143225-04-1P 145708-16-3P,
6-Benzothiazolesulfonic acid 157566-75-1P 157566-99-9P
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251113-84-5P 251113-89-0P 251113-90-3P 251113-91-4P
251113-92-5P 251113-93-6P 251113-94-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(benzo fused heterocyclo sulfonyl halide intermediates
for the preparation of amino acids as HIV protease inhibitors)

INDEX TERM: 181289-52-1P 181289-53-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(benzo fused heterocyclo sulfonyl halide intermediates
for the preparation of amino acids as HIV protease inhibitors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Lilly; EP 0583960 A 1994 CAPLUS
(2) Searle; WO 9622287 A 1996 CAPLUS
(3) Searle; WO 9628418 A 1996 CAPLUS
(4) Searle; WO 9718205 A 1997 CAPLUS

REFERENCE 7

ACCESSION NUMBER: 131:337352 CA
TITLE: Preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; DeCrescenzo, Gary A.; Freskos, John

N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 401,838, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-36
SECONDARY: A61K031-415; C07D317-62; C07D277-62
US PATENT CLASSIF.: 514228200
CLASSIFICATION: 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5985870	A	19991116	US 1997-913069	19971219
WO 9628418	A1	19960919	WO 1996-US2682	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 6380188	B1	20020430	US 2000-672449	20000929
US 2003191166	A1	20031009	US 2002-82123	20020226
US 6667307	B2	20031223		
US 2004147758	A1	20040729	US 2003-677729	20031003
US 7045518	B2	20060516		

PRIORITY APPLN. INFO.:
US 1995-401838 19950310
WO 1996-US2682 19960307
US 1995-478625 19950607
US 1997-913069 19971219
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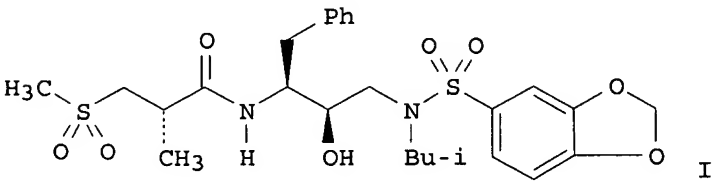

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ABSTRACT:
Sulfonylalkanoylamino hydroxyethylamino sulfonamide compds. R5S(O)t(CH2)nCHR1CONHCHR2CH(OH)CH2NR3SO2R4 (R1 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2SOMe, CH2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = benzo-fused heteroaryl or heterocyclyl; n, t = 0-2) were prepared as retroviral protease inhibitors. Thus, N-[2R-hydroxy-3-[(2-methylpropyl)[(1,3-benzodioxol-5-yl)sulfonyl]amino]-1S-(phenylmethyl)propyl]-2S-methyl-3-

(methylsulfonyl)propanamide (I) was prepared and assayed for HIV protease inhibitory activity (IC50 = 2 nM; EC50 = 20 nM).

SUPPL. TERM: sulfonylalkanoylamino hydroxyethylamino sulfonamide prepn protease inhibitors; benzodioxolesulfonamide sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzofuransulfonamide sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzothiazolesulfonamide sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor; benzodioxanesulfonamide sulfonylalkanoylaminohydroxyalkyl prepn retroviral protease inhibitor

INDEX TERM: AIDS (disease)
Anti-AIDS agents
Antiviral agents
Human immunodeficiency virus 1
Retroviridae
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 144114-21-6, Retropepsin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(HIV; preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 174303-66-3P 183004-72-0P 183004-73-1P 183004-74-2P 183004-78-6P 183182-29-8P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 9001-92-7, Protease
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions 74-97-5, Bromochloromethane 78-81-9, Isobutylamine 96-33-3 98-74-8, 4-Nitrobenzenesulfonyl chloride 100-52-7, Benzaldehyde, reactions 107-10-8, Propylamine, reactions 107-85-7, Isoamylamine 109-73-9, Butylamine, reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride 274-09-9, 1,3-Benzodioxole 333-20-0, Potassium thiocyanate 593-71-5, Chloroiodomethane 3182-95-4, L-Phenylalaninol 4224-69-5, Methyl 2-(bromomethyl)acrylate 4410-99-5, Phenethyl mercaptan 10605-21-7 20609-71-6, Methyl 3-bromo-2-methylpropionate 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 26049-94-5 63758-12-3, 1,4-Benzodioxan-6-sulfonyl chloride 74431-52-0 76497-39-7 81000-54-6 116661-86-0 143224-62-8 181124-54-9 201683-41-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 496-16-2P, 2,3-Dihydrobenzofuran 1718-39-4P 18101-58-1P 36525-60-7P, 2-(Methylsulfonylmethyl)acrylic acid 42807-45-4P 79213-74-4P 81026-69-9P 111060-52-7P 111060-64-1P 111060-81-2P 111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 128018-43-9P 128018-44-0P 143224-81-1P 143224-92-4P 143224-94-6P, Methyl 2-(methylsulfonylmethyl)acrylate

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ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

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ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of sulfonylalkanoylamino hydroxyethylamino sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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(10) Anon; EP 0342541 1989 CAPLUS
(11) Anon; EP 0346847 1989 CAPLUS
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(13) Anon; EP 0356223 1990 CAPLUS
(14) Anon; EP 0389898 1990 CAPLUS
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(16) Anon; EP 0393457 1990 CAPLUS
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(18) Anon; EP 0468641 1992 CAPLUS
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(62) Vazquez; US 5760064 1998 CAPLUS

REFERENCE 8

ACCESSION NUMBER: 131:286828 CA
TITLE: Preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan R.; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 96 pp., Cont.-in-part of U.S. Ser. No. 402,287, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-40
SECONDARY: C07D207-06
US PATENT CLASSIF.: 514422000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968970	A	19991019	US 1998-894900	19980102
WO 9628463	A1	19960919	WO 1996-US2684	19960307

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
EP 1258491 A1 20021120 EP 2002-11526 19960307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI
US 2002111368 A1 20020815 US 2001-836443 20010418
US 6458785 B2 20021001
PRIORITY APPLN. INFO.: US 1995-402287 19950310
WO 1996-US2684 19960307
US 1995-474052 19950607
EP 1996-907135 19960307
US 1999-451920 19991201

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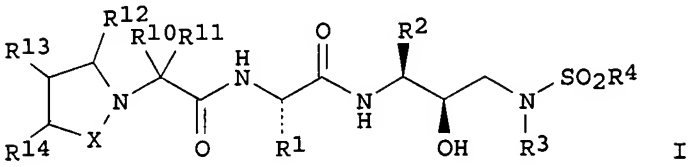

I

ABSTRACT:
Amino acid hydroxyethylamino sulfonamide compds. I [X = CH2, CH2CH2; R1 = alkyl, alkenyl, alkynyl, hydroxy-, alkoxy-, or cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SO2NH2, CH2SMe, CH2S(O)Me, CH2SO2Me, CMe2SMe, CMe2S(O)Me, CMe2SO2Me; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl; R10 = H, alkyl, hydroxy- or alkoxyalkyl; R11 = H, alkyl, hydroxyalkyl, alkoxyalkyl, benzyl, imidazolylmethyl, CH2CH2CONH2, CH2CONH2, CH2CH2SMe, CH2SMe, CH2S(O)Me, CH2SO2Me; R12 = H, hydroxyalkyl, alkoxyalkyl; R13, R14 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, or alkoxyalkyl or R13 and R14 together form (un)substituted benzo or heteroaryl] or their pharmaceutically acceptable salts, prodrugs, or esters were prepared as retroviral protease inhibitors. Thus, 2S-(pyrrolidinoacetamido)-N-[2R-hydroxy-3-[N1-(2-methylpropyl)-N1-(2,3-dihydrobenzofuran-5-ylsulfonyl)amino]-1S-(phenylmethyl)propyl]-3S-methylpentanamide was prepared and showed IC50 = 2 nM for inhibition of HIV protease.

SUPPL. TERM: amino acid hydroxyethylamino sulfonamide prepn retroviral protease inhibitor

INDEX TERM: Antiviral agents
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: Amino acids, preparation
Peptides, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 144114-21-6, Retropepsin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 183812-51-3P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 174303-65-2P 183553-47-1P 183553-66-4P 183553-78-8P
183553-82-4P 183553-86-8P 183553-87-9P 183553-89-1P
183553-94-8P 183554-03-2P 183554-04-3P 183554-05-4P
183554-07-6P 183554-15-6P 183594-99-2P 183812-50-2P
183812-53-5P

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 144114-21-6, Retropepsin

ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions
74-97-5, Bromochloromethane 78-81-9, Isobutylamine
98-68-0, 4-Methoxybenzenesulfonyl chloride 98-74-8,
4-Nitrobenzenesulfonyl chloride 100-52-7, Benzaldehyde,
reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride
123-75-1, Pyrrolidine, reactions 274-09-9,
1,3-Benzodioxole 496-16-2, 2,3-Dihydrobenzofuran
541-88-8, Chloroacetic anhydride 593-71-5,
Chloroiodomethane 3182-95-4, L-Phenylalaninol 5292-43-3,
tert-Butyl bromoacetate 10605-21-7 26049-94-5
63758-12-3 112898-23-4 116661-86-0 143225-04-1
157566-91-1 159005-61-5 181124-54-9 208394-11-0

ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)

INDEX TERM: 1718-39-4P, n-(4-Sulfonamidophenyl)thiourea 6628-74-6P,
1-Pyrrolidineacetic acid hydrochloride 18101-58-1P
42807-45-4P 79213-74-4P 111060-52-7P 111060-64-1P
111138-83-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl
chloride 115010-11-2P 127927-43-9P 128018-43-9P
128018-44-0P 143224-62-8P 145708-16-3P,
6-Benzothiazolesulfonic acid 149451-80-9P 149451-81-0P
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ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)
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ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of amino acid hydroxyethylamino sulfonamides as retroviral protease inhibitors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD.
REFERENCE(S): (1) Getman; US 5756533 1998 CAPLUS
(2) Vasquez; J Med Chem 1995, V38(4), P582

REFERENCE 9

ACCESSION NUMBER: 129:122867 CA
TITLE: Heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; DeCrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 75 pp., Cont.-in-part of U. S. Ser. No. 402,419, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-40
SECONDARY: C07D207-48
US PATENT CLASSIF.: 514422000
CLASSIFICATION: 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27, 28
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776971	A	19980707	US 1995-474117	19950607
CA 2215022	AA	19960919	CA 1996-2215022	19960307
WO 9628465	A1	19960919	WO 1996-US2683	19960307
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AU 9654178	A1	19961002	AU 1996-54178	19960307
AU 717598	B2	20000330		
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CN 1183102	A	19980527	CN 1996-193619	19960307
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RU 2174519	C2	20011010	RU 1997-116523	19960307
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US 2004198989	A1	20041007	US 2003-715852	20031119

PRIORITY APPLN. INFO.:

US 1995-402419 19950310
US 1995-392305 19950410
US 1995-474117 19950607
WO 1996-US2683 19960307
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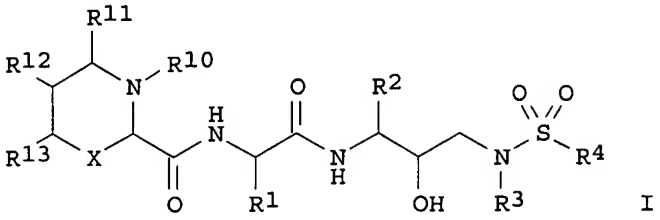

I

ABSTRACT:
Heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide compds. I (X = bond or CH2; R1 = H, alkyl, alkenyl, alkynyl, imidazolylmethyl, CH2CONH2, CH2SO2NH2, etc.; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl, etc.; R10 = H, alkyl, benzyl, phenylmethoxycarbonyl, tert-butoxycarbonyl, 4-methoxyphenylmethoxycarbonyl; R11 = H, hydroxyalkyl, alkoxyalkyl; R12, R13 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, alkoxyalkyl; or R11 and R12 or R12 and R13 are optionally substituted benzo radical) were prepared as retroviral protease inhibitors. Thus, 2S-[[(pyrrolidin-2-yl)carbonyl]amino]-N-[2R-hydroxy-3-[[(1,3-benzodioxol-5-yl)sulfonyl](2-methylpropyl)amino]-1S-(phenylmethyl)propyl]-3,3-dimethylbutanamide was assayed for protease inhibitory activity (IC50 = 2 nM, EC50 = 12 nM).

SUPPL. TERM: heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide prepn; protease inhibitor heterocyclyl amino acid

INDEX TERM: Human immunodeficiency virus 1
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Amino acids, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 183581-21-7P 183581-22-8P 183581-23-9P 183581-24-0P
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183813-28-7P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 9001-92-7, Protease
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions
78-81-9, Isobutylamine 98-68-0, 4-Methoxybenzenesulfonyl chloride 274-09-9, 1,3-Benzodioxole 496-16-2, 2,3-Dihydrobenzofuran 937-32-6, 4-Nitrobenzenesulfenyl chloride 3182-95-4, L-Phenylalaninol 10605-21-7
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63758-12-3, 1,4-Benzodioxan-6-sulfonyl chloride
116661-86-0 143224-62-8 159005-61-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 1718-39-4P 18101-58-1P 42807-45-4P, N-Benzyl-L-phenylalaninol 79213-74-4P 111060-52-7P 111060-64-1P
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ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

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183005-03-0P 183553-43-7P 183553-92-6P 183553-96-0P
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ROLE: SPN (Synthetic preparation); PREP (Preparation)
(heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
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(23) Anon; WO 9410134 1994 CAPLUS
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REFERENCE 10

ACCESSION NUMBER: 129:41411 CA
TITLE: Preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors
INVENTOR(S): Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Devadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 93 pp., Cont.-in-part of U. S. Ser. No. 402,287, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-40
SECONDARY: C07D207-06
US PATENT CLASSIF.: 514422000
CLASSIFICATION: 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756533	A	19980526	US 1995-474052	19950607
CA 2215061	AA	19960919	CA 1996-2215061	19960307
WO 9628463	A1	19960919	WO 1996-US2684	19960307
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9650294	A1	19961002	AU 1996-50294	19960307
AU 705268	B2	19990520		
EP 813542	A1	19971229	EP 1996-907135	19960307
EP 813542	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1186499	A	19980701	CN 1996-193620	19960307
JP 2001513746	T2	20010904	JP 1996-527648	19960307
AT 226213	E	20021115	AT 1996-907135	19960307
EP 1258491	A1	20021120	EP 2002-11526	19960307
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PT 813542	T	20030131	PT 1996-907135	19960307
ES 2187640	T3	20030616	ES 1996-907135	19960307
EE 4349	B1	20040816	EE 1997-201	19960307
NO 9704148	A	19971027	NO 1997-4148	19970909
US 5965601	A	19991012	US 1998-33897	19980303
US 6140505	A	20001031	US 1998-80928	19980519
US 6310080	B1	20011030	US 1999-451920	19991201
US 2002111368	A1	20020815	US 2001-836443	20010418
US 6458785	B2	20021001		
US 2003216435	A1	20031120	US 2002-200589	20020723
US 6730669	B2	20040504		
US 2004260095	A1	20041223	US 2004-760125	20040120

PRIORITY APPLN. INFO.:
US 1995-402287 19950310
US 1995-391873 19950222
US 1995-474052 19950607
EP 1996-907135 19960307
WO 1996-US2684 19960307
US 1998-80928 19980519
US 1999-451920 19991201
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US 2002-200589 20020723

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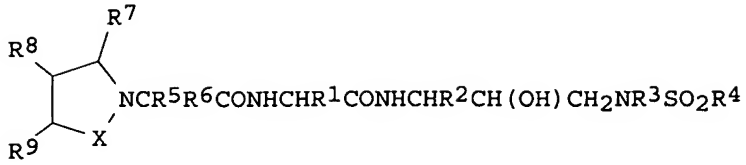

I

ABSTRACT:
Amino acid hydroxyethylamino sulfonamide compds. I (X = CH2 or CH2CH2; R1 = alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cyanoalkyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2SMe, CMe2SMe or their sulfone or sulfoxide derivative; R2 = alkyl, aralkyl, alkylthioalkyl, arylthioalkyl, cycloalkylalkyl; R3 = alkyl, cycloalkyl, cycloalkylmethyl; R4 = aryl, benzo-fused heteroaryl or heterocyclyl; R5 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R6 = H, alkyl, hydroxyalkyl, alkoxyalkyl, benzyl, imidazolylmethyl, CH2CONH2, CH2CH2CONH2, CH2CH2SMe, CH2SMe or their sulfone or sulfoxide derivs.; R7 = H, hydroxyalkyl, alkoxyalkyl; R8, R9 = H, OH, alkoxy, 2-hydroxyethoxy, hydroxyalkyl, alkoxyalkyl; or R7 and R8 or R8 and R9 form a heteroaryl or benzo radical) were prepared as retroviral protease inhibitors. Thus, 2S-[(pyrrolidin-1-yl)acetylamino]-N-[2R-hydroxy-3-[N1-(2-methylpropyl)-N1-(2,3-dihydrobenzofuran-5-ylsulfonyl)amino]-1S-(phenylmethyl)propyl]-3S-methylpentanamide, prepared from N-[3S-benzyloxycarbonylamino-2R-hydroxy-4-phenylbutyl]-N-isobutylamine, tert-Bu bromoacetate, pyrrolidine, and 2,3-dihydrofuran, showed HIV protease inhibitory activity IC50 = 2 nM.

SUPPL. TERM: amino acid hydroxyethylamino sulfonamide prepn HIV; protease inhibitor amino acid sulfonamide

INDEX TERM: Human immunodeficiency virus
(preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: Amino acids, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 174303-65-2P 183553-47-1P 183553-66-4P 183553-78-8P
183553-82-4P 183553-86-8P 183553-87-9P 183553-89-1P
183553-94-8P 183554-03-2P 183554-04-3P 183554-05-4P
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183554-68-9P 183554-70-3P 183594-99-2P 183812-50-2P
183812-51-3P 183812-53-5P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 9001-92-7, Protease
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

INDEX TERM: 63-74-1, Sulfanilamide 63-91-2, L-Phenylalanine, reactions 78-81-9, Isobutylamine 79-11-8, reactions 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-74-8, 4-Nitrobenzenesulfonyl chloride 100-52-7, Benzaldehyde,

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3-Nitrobenzenesulfonyl chloride 123-75-1, Pyrrolidine,
reactions 274-09-9, 1,3-Benzodioxole 333-20-0, Potassium
thiocyanate 496-16-2, 2,3-Dihydrobenzofuran 1149-26-4
3160-59-6 3182-95-4, L-Phenylalaninol 3392-08-3
5292-43-3, tert-Butyl bromoacetate 10605-21-7,
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[(phenylmethoxy)carbonyl]- 63039-48-5 63758-12-3
112898-23-4 116661-86-0 157446-10-1 157566-91-1
159005-61-5 181124-54-9 183554-30-5 208394-11-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamide
retroviral protease inhibitors)

INDEX TERM: 1718-39-4P 6628-74-6P, 1-Pyrrolidineacetic acid
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111060-52-7P 111060-64-1P 111138-83-1P 115010-10-1P,
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ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of amino acid hydroxyethylamino sulfonamide
retroviral protease inhibitors)

INDEX TERM: 157445-95-9P 157566-75-1P 158380-76-8P 159006-12-9P
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183554-33-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of amino acid hydroxyethylamino sulfonamide
retroviral protease inhibitors)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Anon; EP 0104041 1984 CAPLUS
(2) Anon; EP 0114993 1984 CAPLUS
(3) Anon; WO 840304 1984
(4) Anon; EP 0172347 1986 CAPLUS
(5) Anon; EP 0223437 1987 CAPLUS
(6) Anon; GB 2184730 1987 CAPLUS
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(13) Anon; EP 0356223 1990 CAPLUS
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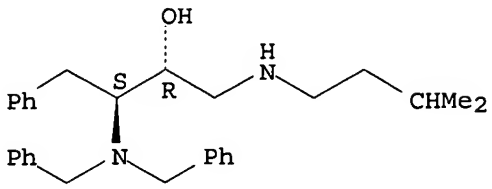
(54) Silcox; J Heterocycl Chem 1967, V4, P166

L2 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 170359-26-9 REGISTRY
ED Entered STN: 17 Nov 1995
CN Benzenepropanol, β-[bis(phenylmethyl)amino]-α-[[(3-methylbutyl)amino]methyl]-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H38 N2 O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.18	3

Absolute stereochemistry.



Predicted Properties (PPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	34.09	pH 1 25 deg C	(1)
Bioconc. Factor (BCF)	34.09	pH 2 25 deg C	(1)
Bioconc. Factor (BCF)	34.17	pH 3 25 deg C	(1)
Bioconc. Factor (BCF)	34.92	pH 4 25 deg C	(1)
Bioconc. Factor (BCF)	42.51	pH 5 25 deg C	(1)
Bioconc. Factor (BCF)	121.95	pH 6 25 deg C	(1)
Bioconc. Factor (BCF)	1010.70	pH 7 25 deg C	(1)
Bioconc. Factor (BCF)	10031.08	pH 8 25 deg C	(1)
Bioconc. Factor (BCF)	83016.36	pH 9 25 deg C	(1)
Bioconc. Factor (BCF)	302364.47	pH 10 25 deg C	(1)
Boiling Point (BP)	577.8+/-50.0 deg C	760 Torr	(1)
Density (DEN)	1.058+/-0.06 g/cm**3	760 Torr	(1)
Enthalpy of Vap. (HVAP)	90.98+/-3.0 kJ/mol	760 Torr	(1)
Flash Point (FP)	303.2+/-30.1 deg C		(1)
Freely Rotatable Bonds (FRB)	14		(1)
H acceptors (HAC)	3		(1)
H donors (HD)	2		(1)
Hydrogen Donors/Acceptors Sum (HDAS)	5		(1)
Koc (KOC)	29.74	pH 1 25 deg C	(1)
Koc (KOC)	29.74	pH 2 25 deg C	(1)
Koc (KOC)	29.81	pH 3 25 deg C	(1)
Koc (KOC)	30.47	pH 4 25 deg C	(1)
Koc (KOC)	37.09	pH 5 25 deg C	(1)
Koc (KOC)	106.39	pH 6 25 deg C	(1)
Koc (KOC)	881.77	pH 7 25 deg C	(1)
Koc (KOC)	8751.43	pH 8 25 deg C	(1)
Koc (KOC)	72426.12	pH 9 25 deg C	(1)
Koc (KOC)	263792.41	pH 10 25 deg C	(1)
logD (LOGD)	3.61	pH 1 25 deg C	(1)
logD (LOGD)	3.61	pH 2 25 deg C	(1)
logD (LOGD)	3.61	pH 3 25 deg C	(1)
logD (LOGD)	3.62	pH 4 25 deg C	(1)
logD (LOGD)	3.71	pH 5 25 deg C	(1)
logD (LOGD)	4.17	pH 6 25 deg C	(1)
logD (LOGD)	5.09	pH 7 25 deg C	(1)
logD (LOGD)	6.08	pH 8 25 deg C	(1)
logD (LOGD)	7.00	pH 9 25 deg C	(1)
logD (LOGD)	7.56	pH 10 25 deg C	(1)
logP (LOGP)	7.714+/-0.724	25 deg C	(1)

Mass Intrinsic Solubility (ISLB.MASS)	0.000095 g/L	25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 1 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 2 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 3 25 deg C	(1)
Mass Solubility (SLB.MASS)	1.2 g/L	pH 4 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.95 g/L	pH 5 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.34 g/L	pH 6 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.041 g/L	pH 7 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0041 g/L	pH 8 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00052 g/L	pH 9 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00014 g/L	pH 10 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.0037 g/L	Unbuffered Water pH 8.05 25 deg C	(1)
Molar Intrinsic Solubility (ISLB.MOL)	0.00000022 mol/L	25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0028 mol/L	pH 1 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0028 mol/L	pH 2 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0028 mol/L	pH 3 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0027 mol/L	pH 4 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0022 mol/L	pH 5 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00078 mol/L	pH 6 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.000095 mol/L	pH 7 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000095 mol/L	pH 8 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000012 mol/L	pH 9 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.00000032 mol/L	pH 10 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000086 mol/L	Unbuffered Water pH 8.05 25 deg C	(1)
Molar Volume (MVOL)	406.9+/-3.0 cm**3/mol	20 deg C 760 Torr	(1)
Molecular Weight (MW)	430.62		(1)
pKa (PKA)	14.30+/-0.20	Most Acidic 25 deg C	(1)
pKa (PKA)	9.62+/-0.29	Most Basic 25 deg C	(1)
Polar Surface Area (PSA)	35.50 A**2		(1)
Vapor Pressure (VP)	3.42E-14 Torr	25 deg C	(1)

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.14 ((C) 1994-2006 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 125:221368 CA
TITLE: Method of preparing retroviral protease inhibitor intermediates via diastereomer purification
INVENTOR(S): Ng, John S.; Przybyla, Claire A.; Zhang, Shu-Hong
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07C213-10
SECONDARY: C07C213-00; C07C215-28
CLASSIFICATION: 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 45

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622275	A1	19960725	WO 1996-US918	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 5831117	A	19981103	US 1995-376340	19950120
CA 2210973	AA	19960725	CA 1996-2210973	19960118
AU 9647653	A1	19960807	AU 1996-47653	19960118
AU 692062	B2	19980528		
BR 9606981	A	19971104	BR 1996-6981	19960118
EP 804410	A1	19971105	EP 1996-903641	19960118
EP 804410	B1	20010829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
CN 1177955	A	19980401	CN 1996-192444	19960118
JP 10512571	T2	19981202	JP 1996-522442	19960118
AT 204851	E	20010915	AT 1996-903641	19960118
ES 2162650	T3	20020101	ES 1996-903641	19960118
PT 804410	T	20020130	PT 1996-903641	19960118
CN 1623977	A	20050608	CN 2004-10056028	19960118
US 6201150	B1	20010313	US 1998-24662	19980217
US 2001047111	A1	20011129	US 2000-741087	20001221
US 6515162	B2	20030204		
US 2003171612	A1	20030911	US 2002-325952	20021223
US 2005131075	A1	20050616	US 2004-961405	20041012
US 7060851	B2	20060613		
PRIORITY APPLN. INFO.:			US 1995-376340	19950120
			WO 1996-US918	19960118
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			US 2000-741087	20001221
			US 2002-325952	20021223

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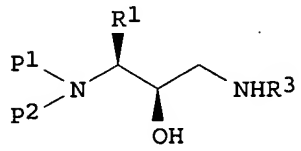

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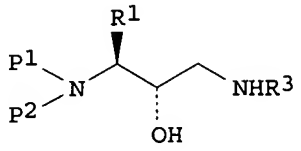

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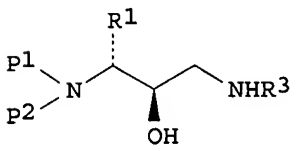

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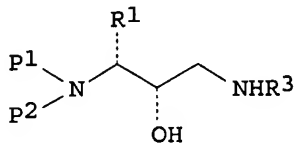

IV

ABSTRACT:
The title compds. [I-IV; P1, P2 = H, acyl, aralkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, , etc.; R1 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, (un)substituted aralkyl; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, heteroaryl, aryl, etc.], useful as pharmaceutical

intermediates (no data), are prepared and crystallized from solution in the form of a
salt (i.e., organic acid and inorg. acid salts of the amine intermediates). The
method is suitable for large-scale (i.e., multi-kilogram) production

SUPPL. TERM: chiral phenylhydroxyurea resoln
INDEX TERM: Isosteric compounds
Resolution
(method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: Ligroine
ROLE: NUU (Other use, unclassified); USES (Uses)
(solvent; method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: Alcohols, preparation
ROLE: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(amino, method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: 143224-89-9P 170359-23-6P
ROLE: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: 64-19-7DP, Acetic acid, salts 75-75-2DP, Methanesulfonic acid, salts 76-05-1DP, Trifluoroacetic acid, salts 87-69-4DP, Tartaric acid, salts 90-64-2DP, Mandelic acid, salts 104-15-4DP, Toluenesulfonic acid, salts 144-62-7DP, Oxalic acid, salts 3144-16-9DP, Camphorsulfonic acid, salts 6915-15-7DP, Malic acid, salts 7647-01-0DP, Hydrochloric acid, salts 7664-38-2DP, Phosphoric acid, salts 7664-93-9DP, Sulfuric acid, salts 7782-99-2DP, Sulfurous acid, salts 10035-10-6DP, Hydrobromic acid, salts 42807-45-4P 111060-52-7P 111060-64-1P 111138-83-1P 118970-37-9P 127927-43-9P 127943-39-9P 143224-64-0P 149451-80-9P 149451-81-0P 153380-32-6P 158380-73-5P 158380-76-8P 160232-08-6P 168056-78-8P 169331-42-4P 170359-14-5P 170359-16-7P 170359-18-9P 170359-22-5P 170359-24-7P 170359-26-9P 170359-27-0P 171370-12-0P 174391-93-6P 181023-00-7P 181023-01-8P 181289-50-9P 181289-51-0P 181289-52-1P 181289-53-2P 181289-54-3P
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: 78-81-9, Isobutylamine 78-84-2, Isobutyraldehyde 79-37-8, Oxalyl chloride 98-59-9, Toluenesulfonyl chloride 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 107-85-7, Isoamylamine 109-72-8, n-Butyl lithium, reactions 590-86-3, Isovaleraldehyde 1609-86-5, tert-Butyl isocyanate 1774-47-6, Trimethylsulfoxonium iodide 24424-99-5, Di-tert-butyl dicarbonate 116661-86-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(method of preparing retroviral protease inhibitor intermediates via diastereomer purification)
INDEX TERM: 56-23-5, Carbon tetrachloride, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 75-09-2, Dichloromethane, uses 108-88-3, Toluene, uses 109-99-9, Thf, uses 110-54-3, Hexane, uses 115-10-6, Dimethyl ether 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 1330-20-7, Xylene,

uses 1634-04-4, Mtbe
ROLE: NUU (Other use, unclassified); USES (Uses)
(solvent; method of preparing retroviral protease inhibitor intermediates via diastereomer purification)

REFERENCE 2

ACCESSION NUMBER: 123:339376 CA
TITLE: Preparation of diaminoalcohols as retroviral protease inhibitor intermediates
INVENTOR(S): Ng, John S.; Przybyla, Claire A.; Mueller, Richard A.; Vasquez, Michael L.; Getman, Daniel P.; Freskos, John J.; Decrescenzo, Gary A.; Bertenshaw, Deborah E.; Heintz, Robert M.; et al.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; et al.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07C215-28
SECONDARY: C07C301-02; C07D301-02; C07D303-36; C07C221-00; C07C223-02; C07C269-04; C07C271-20; C07C213-08
CLASSIFICATION: 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514653	A1	19950601	WO 1994-US12201	19941031
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9510833	A1	19950613	AU 1995-10833	19941031
EP 730570	A1	19960911	EP 1995-901697	19941031
EP 730570	B1	20000419		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 855388	A2	19980729	EP 1998-103779	19941031
EP 855388	A3	19990714		
EP 855388	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 191907	E	20000515	AT 1995-901697	19941031
ES 2145252	T3	20000701	ES 1995-901697	19941031
PT 730570	T	20001031	PT 1995-901697	19941031
AT 214046	E	20020315	AT 1998-103779	19941031
PT 855388	T	20020731	PT 1998-103779	19941031
ES 2173520	T3	20021016	ES 1998-103779	19941031
US 5648511	A	19970715	US 1995-452187	19950525
US 5872298	A	19990216	US 1997-833737	19970409
US 5872299	A	19990216	US 1997-854133	19970508
GR 3033429	T3	20000929	GR 2000-401119	20000516
PRIORITY APPLN. INFO.:			US 1993-156498	19931123
			US 1990-615210	19901119
			US 1991-789646	19911114
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			EP 1995-901697	19941031
			WO 1994-US12201	19941031
			US 1995-452187	19950525

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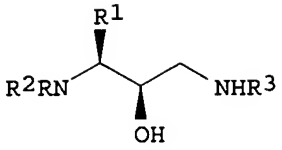

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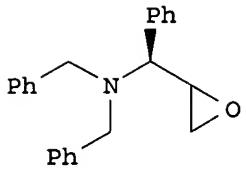

II

ABSTRACT:
Title compds. [I; R, R2 = acyl, aralkyl, alkoxycarbonyl, etc.; R2RN = heterocyclyl; R1 = (cyclo)alkyl, aryl(alkyl), etc.; R3 = H, (cyclo)alkyl, aryl(alkyl), etc.] were prepared Thus, L-phenylalanine was N,N-diprotected and the product reduced to the aminoalc. which was oxidized to give (S)-PhCH2CH[N(CH2PH)2]CHO. The latter was treated with ICH2CL and BuLi in THF at <25° to give an 86:14 mixture of oxiranes (2R)- and (2S)-II the latter of which was condensed with Me2CHCH2NH2 to give I (R = R2 = CH2Ph, R1 = Ph, R3 = CH2CHMe2).

SUPPL. TERM: aminoalc prepn retroviral protease inhibitor intermediate
INDEX TERM: Ring closure and formation
(stereoselective, preparation of diaminoalcs. as retroviral protease inhibitor intermediates)
INDEX TERM: 127943-39-9P 170359-15-6P 170359-19-0P 170359-25-8P
ROLE: BYP (Byproduct); PREP (Preparation)
(preparation of diaminoalcs. as retroviral protease inhibitor intermediates)
INDEX TERM: 42807-45-4P, N-Phenylmethyl-L-phenylalaninol 95437-43-7P, N,N-Bis(phenylmethyl)-L-phenylalanine 99113-35-6P
111060-52-7P 111060-64-1P 127927-43-9P 153380-32-6P
153380-33-7P 158380-73-5P 158380-76-8P 160232-08-6P
169331-42-4P 170359-12-3P 170359-14-5P 170359-16-7P
170359-17-8P 170359-18-9P 170359-20-3P 170359-21-4P
170359-22-5P 170359-24-7P 170359-26-9P 170359-27-0P
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diaminoalcs. as retroviral protease inhibitor intermediates)
INDEX TERM: 168056-78-8P 170359-13-4P 170359-23-6P
ROLE: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of diaminoalcs. as retroviral protease inhibitor intermediates)
INDEX TERM: 63-91-2, L-Phenylalanine, reactions 78-81-9, Isobutylamine 78-84-2, Isobutyraldehyde 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 590-86-3, Isovaleraldehyde 1609-86-5, tert-Butyl isocyanate 3182-95-4, L-Phenylalaninol 116661-86-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diaminoalcs. as retroviral protease inhibitor intermediates)

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